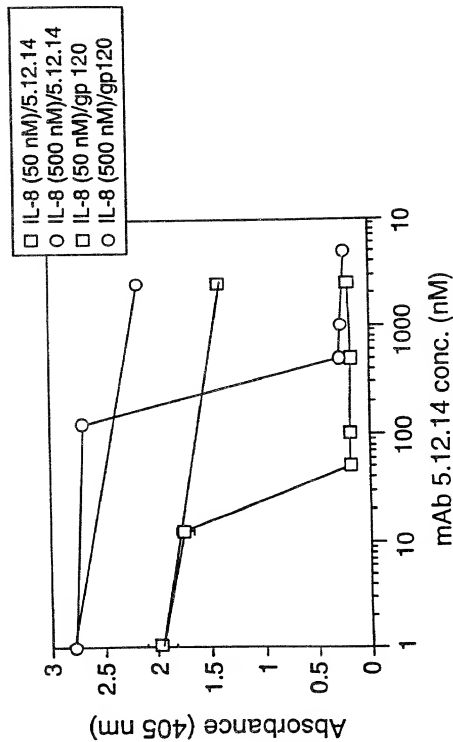
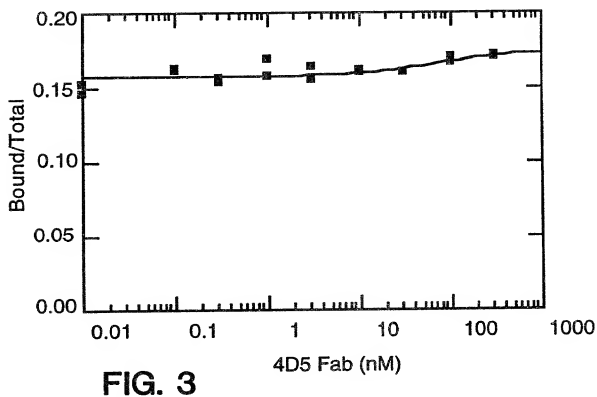
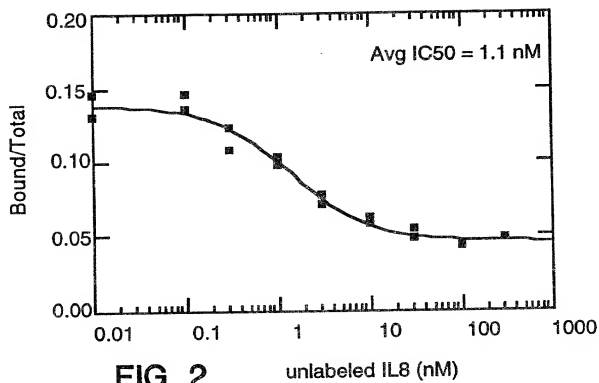


FIG. 1





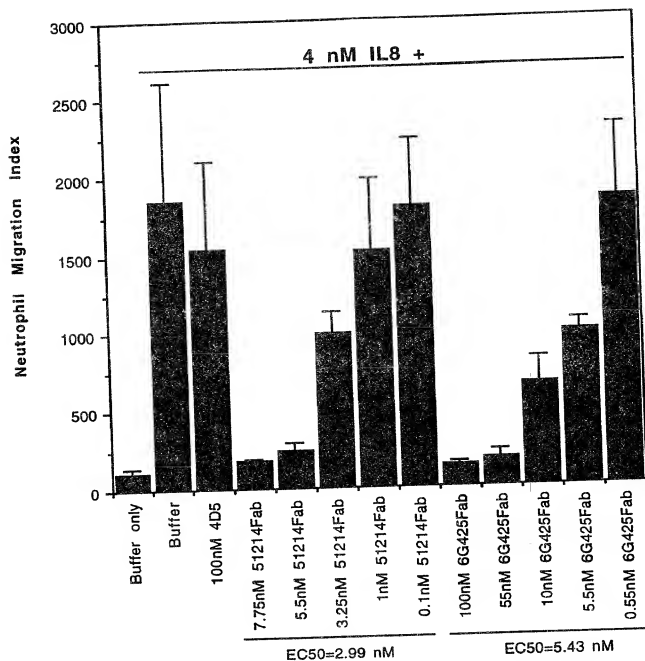


FIG. 6

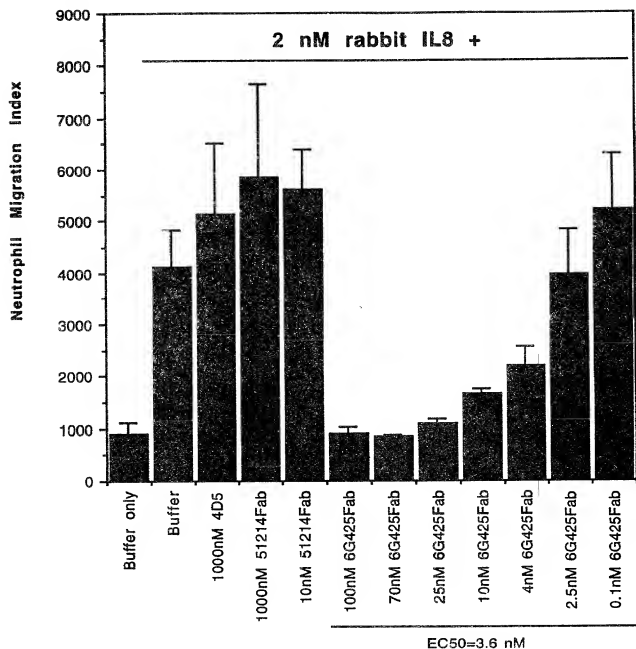


FIG. 7

FIG. 8

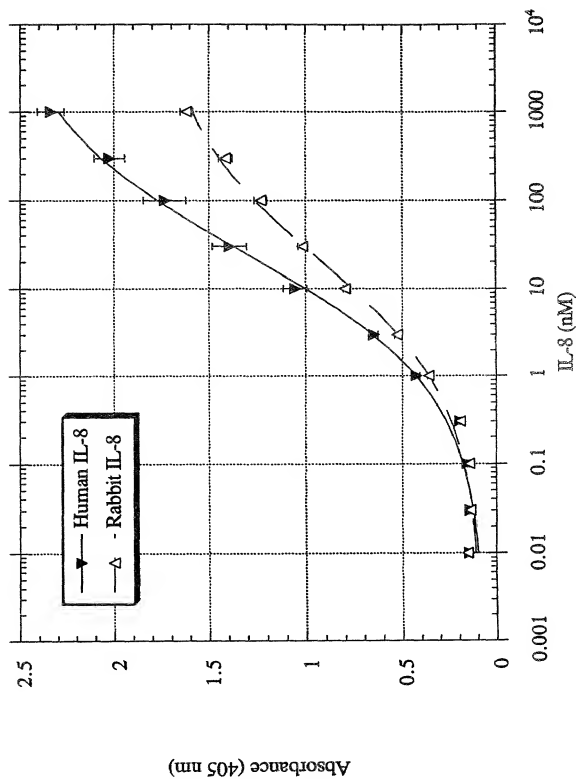


FIG. 9

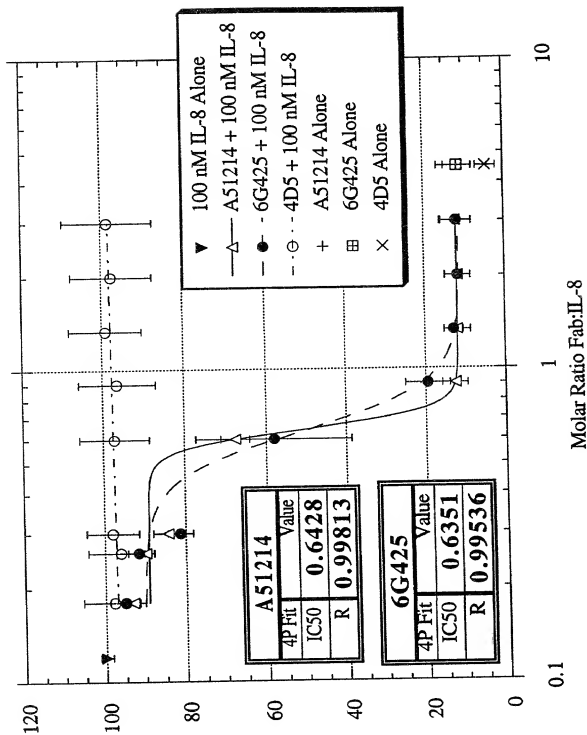
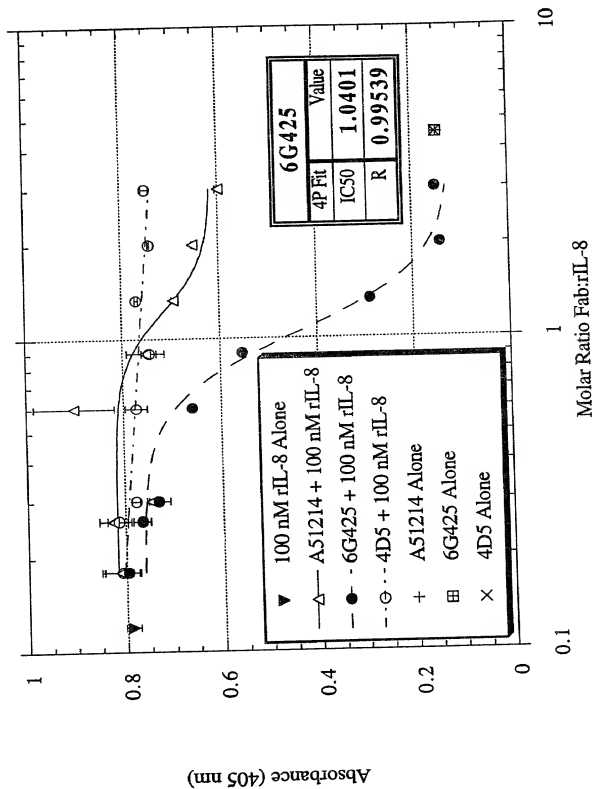


FIG. 10



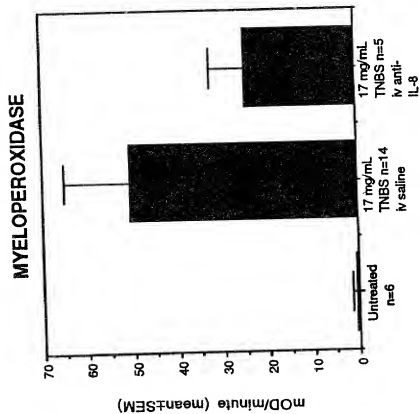


FIG. 11A

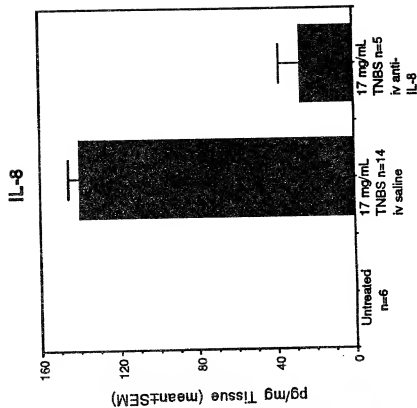


FIG. 11B

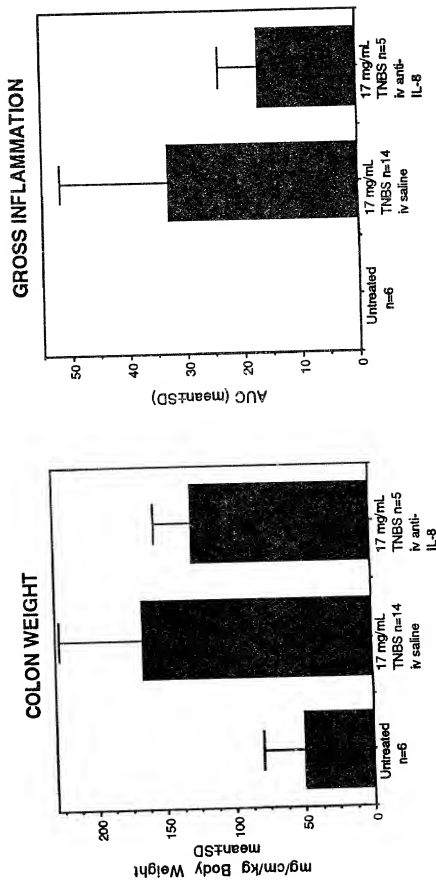


FIG. 11C

FIG. 11D

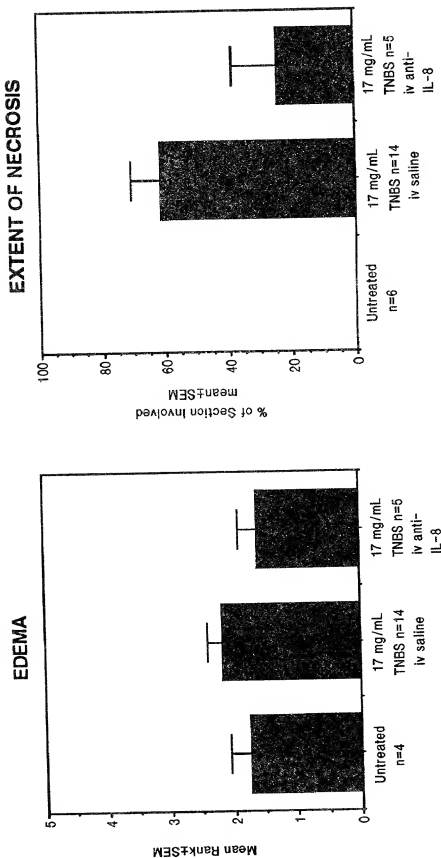


FIG. 11E

FIG. 11F

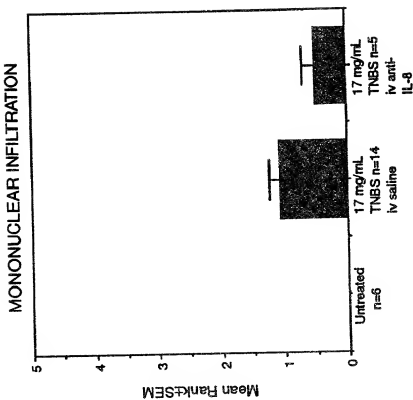


FIG. 11J

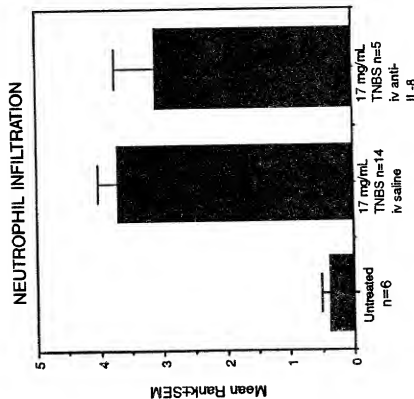
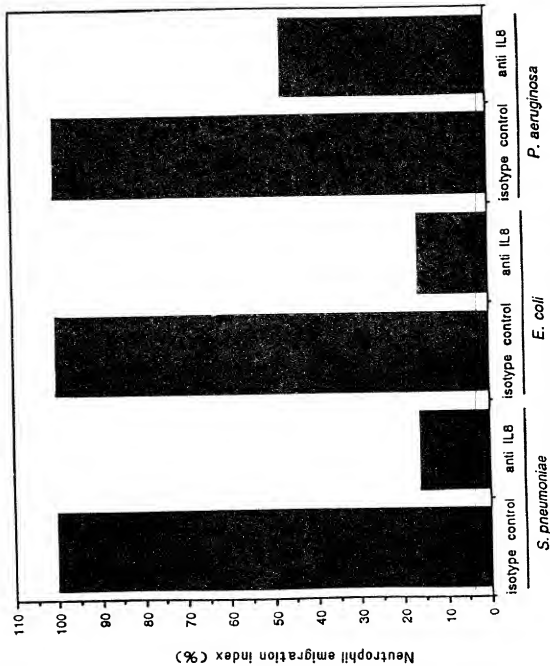


FIG. 11I

FIG. 12



Group (n=5 rabbits per group)

Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAAC TGTTCAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

FIG. 13

FIG. 14

Light chain forward primer

SL001A-2 35 mer

5' ACAACGGCTACGCT GACATCGTCATGACCCAGTC 3' (SEQ ID NO.7)
T T T A
(SEQ ID NO.8)
(SEQ ID NO.9)

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAGATGGATACAGTTGGTGC 3' (SEQ ID NO.10)

FIG. 15

Heavy chain forward primer

SL002B 39 mer

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTGGC 3' (SEQ ID NO.11)
 T C (SEQ ID NO.12)
 G (SEQ ID NO.13)
 A (SEQ ID NO.14)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCGG ATAGACCGATGGGGCTGTTGTTTGGC 3' (SEQ ID NO.11)
 T (SEQ ID NO.15)
 A (SEQ ID NO.14)
 G (SEQ ID NO.13)

1 D I V M T Q S Q K F M S T S V U

21 V T C K A S O N V G T A

CDR #1

41 G Q S P K A L I Y

CGGAAGTGTC CGTCACCTAG ACCCTGTCIA AAGTGAGAGT

ATCCTCTCAC GTT'CGGTC

CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAAG TACCGTATTTT
CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAAG TACCGTATTTT

3

3
3
C

101 G T K L E L K R A D A A A

GGT AAGCTT

16
F/G

1 TTCTATTGCT ACAAACGCGT ACGCTGAGGT GCAGCTGGTG GAGTCTGGGG GAGGCTTAGT
 AAGATAACGA TGT TTGCGCA TGC GACTCCA CGTCGACCAC CTCAGACCCC CTCCGAATCA
 1 E V Q L V E S G G G L V
 61 GCCGCCTGGA GGGTCCCTGA AACTCTCCTG TGCAGCCTCT GGATTCATAT TCAGTAGTTA
 CGGCGGACCT CCCAGGGACT TTGAGAGGAC ACGTCGGAGA CCTAAGTATA AGTCATCAAT
 13 P P G G S L K L S C A A S G F I F S S Y
 * *
 CDR #1
 121 TGGCATGTCT TGGGTTCGCC AGACTCCAGG CAAGAGCCTG GAGTTGGTCG CAACCATTA
 ACCGTACAGA ACCCAAGCGG TCTGAGGTCC GTTCTCGGAC CTC AACCAGC GTTGGAATT
 33 G M S W V R Q T P G K S L E L V A T I N
 * * * * *
 181 TAATAATGGT GATAGCACCT ATTATCCAGA CAGTGTGAAG GGCCGATTCA CCATCTCCCG
 ATTATTACCA CTATCGTGGA TAATAGGTCT GTCAACATTC CCGCTAAGT GGTAGAGGGC
 53 N N G D S T Y Y P D S V K G R F T I S R
 * * * * *
 CDR #2
 241 AGACAATGCC AAGAACACCC TGTACCTGCA AATGAGCAGT CTGAAGTCTG AGGACACAGC
 TCTGTTACGG TTCTTGTGGG ACATGGACGT TTACTCGTCA GACTTCAGAC TCCTGTGTCTG
 73 D N A K N T L Y L Q M S S L K S E D T A
 301 CATGTTTAC TGTGCAAGAG CCCTCATTAG TTCGGCTACT TGGTTTGGTT ACTGGGGCCA
 GTACAAAATG ACAGTTCTC GGGAGTAATC AAGCCGATGA ACCAAACCAA TGACCCCGST
 93 M F Y C A R A L I S S A T W F G Y W G Q
 * * * * *
 CDR #3
 361 AGGGACTCTG GTCACGTCTCT CTGCAGCCAA AACAACAGCC CCATCTGTCT
 TCCCTGAGAC CAGTGACAGA GACGTGGTT TTGTTGTCGG GGTAGACAGA
 113 G T L V T V S A A K T T A P S V Y
 ApaI
 411 ATCCGGG (SEQ ID NO.18)
 TAGGCCC (SEQ ID NO.19)
 130 P

FIG. 17

FIG. 18

VL.front 31-MER

5' ACAAACGCGTACGCTGATATCGTCATGACAG 3' (SEQ ID NO.20)
VL.rear 31-MER

5' GCAGCATCAGCTCTTCGAAGCTCCAGCTTGG 3' (SEQ ID NO.21)

VH.front.SPE 21-MER

5' CCACTAGTACGCAAGTTCACG 3' (SEQ ID NO.22)

VH.rear 33-MER

5' GATGGGCCCTTGGTGGAGGCTGCAGAGACAGTG 3' (SEQ ID NO.23)

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTTCCTAT TGCTACAAAC
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG ATATCGTCAT GACACAGTCT CAAAATTC A TGTCACATC AGTAGGAGAC
CGCATCGCAG TATAGCAGTA CTGTGTCAGA GTTTTAAAGT ACAGGTGTAT TCATCTCTCTG
-3 A Y A D I V M T Q S Q K F M S T S V G D

121 AGGGTCAGCG TCACCTGCAG GCCCAGTCAG AATGTGGGTA CTAATGTAGC CTGGTATCAA
TCCCGATCGC AGTGGACGTT CCGGTCAGTC TTACACCCAT GATTACATCG GACCATAGTT
18 R V S V T C K A S O N V G T N V A W Y Q
* * * * * * * *

CDR #1

181 CAGAAACCGG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCTACCG GTACAGTGGA
GTCTTTGGTC CCTGTAGAGG ATTTCTGAGC TAAATGAGCA GTAGGATGGC CATGTCACCTG
38 Q K P G Q S P K A L I Y S S S Y R Y S G
* * * * *

CDR #2

241 GTCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCAGCCAT
CAGGGACTAG CGAAGTGTCC GTACCTTAGA CCCTGTCTAA AGTGAGAGTG GTAGTCGGTA
58 V P D R F T G S G S G T D F T L T I S H

301 GTGCAGTCTG AAGACTTGGC AGACTATTTT TGTGAGCAAT ATAACATCTA TCCTCTCACG
CTCCTTCAGC TCTTGAACCG TCTGATAAAG ACAGTCTGTTA TATTGTAGAT CAGTACAGTCG
78 V Q S E D L A D Y F C Q Q Y N I Y P L T
* * * * *

CDR #3

BstBI

361 TTCGGTCTCG GGACCAAGCT GGAGCTTCGA AGAGCTGTGG CTGCACCATC TGTCTTCATC
AAGCCAGGAC CCTGGTTCTGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG
98 F G P G T K L E L R R A V A A P S V F I

421 TTCCCGCCAT CTGATGAGCA GTTGAAATCT GGAAGTCTT CTGTTGTGTG CTGCTGAAT
AAGGGCGGTA GACTACTCGT CAACCTTTAGA CCTTGACGAA GACAACACAC GGACGACTTA
118 F P P S D E Q L K S G T A S V V C L L N

481 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCTT CCAATCGGGT
TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTCCGGGA GGTTAGCCCA
138 N F Y P R E A K V Q W K V D N A L Q S G

541 AACTCCAGG AGAGTGTAC AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC
TTGAGGCTCC TCTCACAGTG TCTCGTCTG TCGTTCCTGT CGTGGATGTC GGAGTCGTCTG
158 N S Q E S V T E Q D S K D S T Y S L S S

601 ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCTG CGAAGTCAAC
TGGGACTGCG ACTCGTTTCG TCTGATGCTC TTTGTGTTT AGATGCGGAC GCTTCAGTGG
178 T L T L S K A D Y E K H K V Y A C E V T

661 CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG
GTAGTCCCGG ACTCGAGCGG GCAGTGTGTT TCGAAGTTGT CCCCTCTCAC
198 H Q G L S S P V T K S F N R G E C (SEQ ID NO.25)

711 TTAA (SEQ ID NO.24)
AATT
216 O

FIG. 19

09726550-053104

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N
61 GCGTACGCTG AGGTGCAGCT GGTGGAGTCT GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC
CGCATGCGAC TCCACGTCGA CCACTCAGA CCCCCTCCGA ATCACGGCGG ACCCTCCAGG
-3 A Y A E V Q L V E S G G G L V P P G G S
121 CTGAAACTCT CCTGTGCAGC CTCTGGATTC ATATTAGTA GTTATGGCAT GTCTTGGGTT
GACTTTGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCACCA
18 L K L S C A A S G F I F S S Y G M S W V
* * * *

CDR #1

181 CGCCAGACTC CAGGCAAGAG CCTGGAGTTG GTCGCAACCA TTAATAATAA TGGTGATAGC
GCGGTCTGAG GTCCGTCTCT GGACCTCAAC CAGCGTTGGT AATTATTATT ACCACTATCG
38 R Q T P G K S L E L V A T I N N N G D S
* * * * *
241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC
TGGATAATAG GTCTGTGACA CTTCCTCCGCT AAGTGGTAGA GGGCTCTGTT ACGGTTCTTG
58 T Y Y P D S V K G R F T I S R D N A K N
* * * * *

CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTACTGTGCA
TGGGACATGG ACGTTTACTC GTCAGACTTC AGACTCCTGT GTCCGTACAA AATGACACGT
78 T L Y L Q M S S L K S E D T A M F Y C A
361 AGAGCCCTCA TTAGTTCGGC TACTTGGTTT GGTACTGGG GCCAAGGGAC TCTGGTCACT
TCTCGGGAGT AATCAAGCCG ATGAACCAA CCAATGACCC CGGTTCCCTG AGACCACTGA
98 R A L I S S A T W F G Y W G Q G T L V T
* * * * *

CDR #3

421 GTCTCTGCAG CCTCCACCAA ^{ApaI} GGGCCCATCG GTCTTCCCC TGGCACCCCTC CTCCAAGAGC
CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGTTCTCG
118 V S A A S T K G G P S V F P L A P S S K S
481 ACCTCTGGGG GCACAGCGG CCTGGGCTGC CTGGTCAAGG ACTACTTCCC CGAACCGGTG
TGGAGACCCC CGTGTGCGCG GGACCCGACG GACCACTTCC TGATGAAGGG GCTTGGCCAC
138 T S G G T A A L G C L V K D Y F P E P V
541 ACGGTGTCGT GGAATCAGG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCTTA
TGCCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT
158 T V S W N S G A L T S G V H T F P A V L
601 CAGTCTCTAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC
GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCACTGGC ACGGGAGGTC GTCGAACCCG
178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A

661 ACCGAGCCT ACATCTGCA CGTGAATCAC AAGCCAGCA ACACCAAGGT GGACAAGAA
 TGGGTCTGGA TGTAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT
 198 T Q T Y I C N V N H K P S N T K V D K K
 721 GTTGAGCCCA AATCTTGTGA CAAACTCAC ACATGA (SEQ ID NO.26)
 CAACTCGGT TTGAACACT GTTTGAGTG TGTACT
 218 V E P K S C D K T H T O (SEQ ID NO.27)

FIG. 20B

Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAACTGTT CAGGACGCC 3' (SEQ ID NO.1)

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3' (SEQ ID NO.2)

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3' (SEQ ID NO.3)

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3' (SEQ ID NO.4)

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAATAACCC 3' (SEQ ID NO.5)

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3' (SEQ ID NO.6)

FIG. 21

Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC 3' (SEQ ID NO.28)
 T T T
 A A A

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3' (SEQ ID NO.31)

FIG. 22

Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGGTACGCT GAG ATC CAG CTG CAG CAG 3' (SEQ ID NO.32)
T C (SEQ ID NO.33)

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGCCCCG ATAGACCGATGGGGCTGTGTTTGGC 3' (SEQ ID NO.11)
T (SEQ ID NO.15)
A (SEQ ID NO.14)
G (SEQ ID NO.13)

FIG. 23

70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCTGTGAG TCTTGGAGAT
 C TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
 1 D I V M T Q T P L S L P V S L G D

121 CAGGCTTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGATC ACGGTATTGG AAACACCTAT
 GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCAGAACATG TGCCATAACC TTTGTGGATA
 18 Q A S I S C R S S S O S L V H G I G N T Y
 * * * * * * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
 AATGTAACCA TGGACGTCTT CGGTCCGCTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
 38 L H W Y L Q K P G Q S P K L L I Y K V S
 * * * * *

CDR #2

241 AACCGATTTC CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTCACA
 TTGGCTAAAA GACCCGAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
 58 N R F S G V P D R F S G S G S G T D F T
 * * * * *

301 CTCAGGATCA GCAGAGTGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
 GAGTCCTAGT CGTCTCACT CCGACTCCTA GACCCGTAAA TAAAGACGAG AGTTTCATGT
 78 L R I S R V E A E D L G L Y F C S Q S T
 * * * * *

CDR #3

361 CATGTTCCGC TCACGTTTCG TGCTGGGACC AAGCTGGAGC TGAACGGGC TGATGCTGCA
 GTACAAGGCG AGTGCAAGCC ACGACCTGG TTCGACCTCG ACTTTGCCCG ACTACGACGT
 98 H V P L T F G A G T K L E L K R A D A A
 * * * * *

MunI

421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATGGA (SEQ ID NO.34)
 GGTGTACATA GGTAAGGG TGAGTGTCA CTCGTAACT
 118 P T V S I F P P S S E Q L K (SEQ ID NO.35)

FIG. 24

70 G AGATTCACTGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
C TCTAAGTCGA CGTCGTGAGA CCTGGACTCG ACTACTTCGG ACCCGAAGT
1 E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * * *

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTC'CGG TACCTTTCTC GGAACCTACC TAACCGATGT AACTAGGAAG GTTACCACCT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAC TACATCTGTG TAGAAGGTG
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGAAGTGT AGACTACTGA GACGTGAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCTGA TATCTATGTT GCCGCTGACC AAAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

BstEII
421 GTCACCGTCT CCTCCGCCAA AACCGACAGC CCCATCGGTC TATCCGGGCG
CAGTGGCAGA GGAGGCGGAT TTGGCTGTCT GGGTAGCCAG ATAGGCCCGG
118 V T V S S A K T D S P I G L S G P

471 CATC (SEQ ID NO.36)

GTAG

135 I (SEQ ID NO.37)

FIG. 25

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3' (SEQ ID NO.39)

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3' (SEQ ID NO.40)

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3' (SEQ ID NO.38)

FIG. 26

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAT
TACTTCTTCT TATAGCGTAA AGAAGAAGCT AGATACAAGC AAAAAAGATA ACGATGTTTA
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
CGTATGCGAC TATAGCAGTA CTGTGTCGTG GTGAGAGGG ACGGACAGTC AGAACCTCTA
-3 A Y A D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAAGCTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA

18 Q A S I S C R S S O S L V H G I G N T Y
* * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGCTTT CGGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG

38 L H W Y L Q K P G Q S P K L L I Y K V S
* * * * *

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTT AGTGGCAGTG GATCAGGGAC AGATTTTCACA
TTGGCTAAAA GACCCAGGGT TCTGTCCAAG TCACCGTCCAC CTAGTCCCTG TCTAAAGTGT

58 N R F S G V P D R F S G S G S G T D F T
* * * * *

301 CTCAGGATCA GCAGAGTGGG GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCTTAGT CGTCTCACTT CCGACTCCTA GACCTGAAA TAAAGACGAG AGTTTCTAGT

78 L R I S R V E A E D L G L Y F C S Q S T
* * * * *

CDR #3

361 CATGTTCCGC TCACGTTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGTGTCTGCA
GTACAAGGCG AGTGAAGGCC ACGACCTGG TTCGACCTCG ACTTTGCGCCG AACGAGACGT

98 H V P L T F G A G T K L E L K R A V A A
* * * * *

421 CCAACTGTAT TCATCTTCCC ACCATCCAGT GAGCAATTGA AATCTGGAAC TGCCTCTGTT
GGTTGACATA AGTAGAAGGG TGTAGGTCA CTCGTAACT TTAGACCTTG ACGGAGACAA

118 P T V F I F P P S S E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGAGC ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTACACTT CCACCTATTG

138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACCTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGACC
CGGGAGGTTA GCCCATPTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGT CCGTGTCTGT

158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCCGAGT CGTCGTGGGA CTGCGACTCG TTTGCTCTGA TGCTCTTTGT GTTTCAGATG

178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A

661 GCCTGCGAAG TCACCCATCA GGCCTGAGC TCGCCCGTCA CAAGAGCTT CAACAGGGA
 CGGACGGTTC AGTGGGTAGT CCGGACTCG AGCGGGCAGT GTTTCGAA GTGTCCCT
 198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTAA (SEQ ID NO.41)
 CTCACATT
 218 E C O (SEQ ID NO.42)

FIG. 27B

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTG TTTTTCATAT TGCTACAAAC
TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGATTACAGT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
CGCATGCGAC TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
-3 A Y A E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGTTTAT TCATTTCAGT GCCACTACAT GCACCTGGTG
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
18 V K I S C K A S G Y S F S S H Y M H W V
* * * *

CDR #1

181 AAGCAGAGCC ATGGAAGAG CTTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
TTCGTCCTCG TACCTTTCTC GGAACCTACC TAACCGATGT AACTAGGAAG GTTACCACCT
38 K Q S H G K S L E W I G Y I D P S N G E
* * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAATC GACATCTGTG TAGAAGGTGC
58 T T Y N Q K F K G K A T L T V D T S S S
* * * * *

301 ACAGCCAAAG TGCACTCTAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
TCTCCCTGTA TATCTATGTT GCCGCTGACC AAAAAAGCTAC AGACCCCGCG TCCCTGGTGC
98 R G D Y R Y N G D W F F D V W G A G T T
* * * * *

CDR #3

421 GTCACCGTCT CCTCCGCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCTCC
CAGTGGCAGA GGAGGCGGAG GTGGTTCCCG GTAGCCAGA AGGGGACCG TGGGAGGAGG
118 V T V S S A S T K G P S V F P L A P S S

481 AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA CTTCCCCGAA
TTCCTGTGGA GACCCCGGTG TCGCCGGGAC CCGACGGACC AGTTCTGTAT GAAGGGGCTT
138 K S T S G G T A A L G C L V K D Y F P E

541 CCGGTGACGG TGTCGTGGAA CTCAGCGGCC CTGACCAGCG GCGTGCACAC CTTCCCGGCT
GGCCACTGCC ACAGCACCTT GAGTCCGCGG GACTGGTCGC CGCACGTGTG GAAGGGCCGA
158 P V T V S W N S G A L T S G V H T F P A

601 GTCCTACAGT CCTCAGGACT CTACTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCAGC
CAGGATGTCA GGAGTCCTGA GATGAGGGAG TCGTCGCACC ACTGGCACGG GAGGTGCTCG
178 V L Q S S G L Y S L S S V V T V P S S S

FIG. 28A

661 TTGGGCACCC AGACCTACAT CTGCAAGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC
 AACCGTGGG TCTGGATGTA GACGTGCAC TTAGTGTTCG GGTGTTGTG GTTCCACCTG
 198 L G T Q T Y I C N V N H K P S N T K V D
 721 AAGAAAGTTG AGCCCAATC TTGTGACAAA ACTCAGACAT GA (SEQ ID NO.43)
 TTCTTTCAAC TCGGGTTAG AACACTGTTT TGAGTGTGTA CT
 218 K K V E P K S C D K T H T O (SEQ ID NO.44)

FIG. 28B

Variable Light Chain Domain

10 20 abcde 30 40
6G425 DIVMTQTPLSLFVSLGDAQISCRSSQSLVHGIGNTYLHNYLQKPGQSPKLLIY
 # # # # #
F(ab)-1 DIQMTQSPSSLSASVGDRTVITCRSSQSLVHGIGNTYLHMYQQKPGKAPKLLIY
 # #####
humκ1 DIQMTQSPSSLSASVGDRTVITCRASKTI-----SKYLAWYQQKPGKAPKLLIY
 #####
 ++++++
 L1

50 60 70 80 90 100
6G425 YKVSNRFSGVDFRPSDGSQGTDFLTIRISRVEREDLGLYFCQSQTHVPLTFGAGTKLELKR (SEQ ID NO.45)
 # # # # #
F(ab)-1 YKVSNRFSGVDFRPSDGSQGTDFLTIRISLQPEDPATYYCSQSTHVPLTFGQGTKEIKR (SEQ ID NO.46)
 # # # # #
humκ1 YSGSTLESQVPSRFSQSGSGTDFTLTIRISLQPEDPATYYCQHNEYPLTFGQGTKEIKR (SEQ ID NO.47)
 ===
 ++++++ ++++++
 L2 L3

Variable Heavy Chain Domain

10 20 30 40
6G425 EIQLQQSGPELWPKGASVKISCKASGYFSSHYHMYVQSHGKSLRWI
 # # # # #
F(ab)-1 EVQLVESGGGLVQPGGSLRLSCAASGYFSSHYHMYVQRAPGKGLEWV
 # # # #
humλ1 EVQLVESGGGLVQPGGSLRLSCAASGFSPTCHMHWVRQAPGKGLEWV
 =====
 +++++
 K1

50 a 70 80 abc 90 100 110
6G425 GYIDPSNGETTYNQKFKGKATLTVDTSSTANVHLSLTSDSDSAVYFCAARGDYRYNGDWFFDVNGAGT (SEQ ID NO.48)
 # # # # #
F(ab)-1 GYIDPSNGETTYNQKFKGRFTISRDNKNTLYLQMNLSRAEDTAVYYCAARGDYRYNGDWFFDVNGQGT (SEQ ID NO.49)
 # # # # #
humλ1 GMIHPSDSETRYADSVKGRFTISRDNKNTLYLQMNLSRAEDTAVYYCAARGIVFY-GTTFYFDYWGQGT (SEQ ID NO.50)
 ---- ++++++
 ++++++ ++++++
 H2 H3

FIG. 29

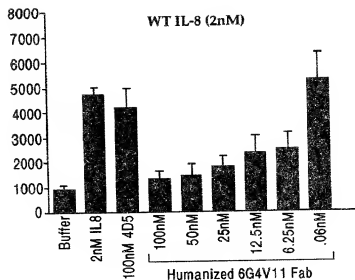


FIG. 30A

IC50~12nM

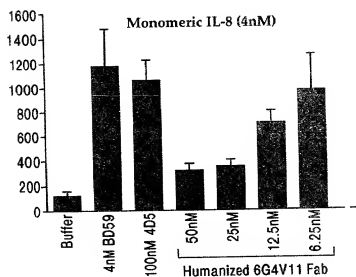


FIG. 30B

IC50~15nM

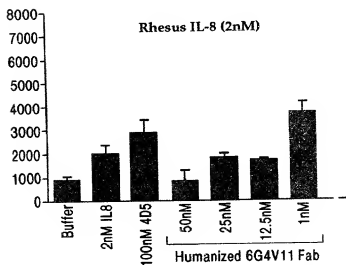


FIG. 30C

IC50~22nM

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

MKKNIAFLIASMFVFSIATNAYADIQMTQSPSLASVSGDRVITTCRSSQSLSLVHGIGNTY
LHWYQQPGKAPKLLIYKVSNRFSGVPSRFSGSGGTDFTLTISLQPEDFATFYCSQST
HVPLTFGGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSSTYSLSSTITLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNIAFLIASMFVFSIATNAYAEVLVQSGGLVQPGGSLRLSCAASGYSFSSHYMH
WYRQAPGKLEWVGVIDPSNGETTYNQFKGRFTISRDNSKNTAYLQMNISLRAEDTAVYY
CARGDYRYNGDWFDFWVGQGLTAVTVSSASTKGPSVFFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVFPPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.52)

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGSGDFDYEKMANANKAMTENADENALQSDAKGLDSVATDYGAAIDGFIGDVVS
GLANGGATGDFAGSNSQMAQVGDGNSPLMNNFRQYLPQLPQSVECRPFVFSAGKPY
EFSIDCDKINLFRGVFAFLLYATFMVYVSTFANILRNKES (SEQ ID NO.53)

FIG. 31A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTTCT TATAGCGTAA AGAAGAAGCT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCGCCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT
TCCAGTGGT AGTGGACGTC CAGTTCAAGT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S Q S L V H G I G N T Y

181 TTCACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGTCTG ACACCGAGCT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGAGC ACTTATTGAA GATAGGTCT CTCCGGTTTC ATGTCACTT CACCACTATT
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGTAATCTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCTGT CCGTGTCTGG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCTGTGGA CTGCGACTCG TTTCTGTTGT TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCAATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGTTT AGTGGGTAGT CCCGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GACTGTTAAG CTGATCTCTT ACGCCGGACG CATCGTGCC CTAGTACGCA ACTAGTCGTA
CTCACAAATC GACTGAGAGA TCGCGGCTCG GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.51)

(SEQ ID NO.54)

FIG. 31B

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

MKKNIAFLIASMFVFSIATNAYADIQMTQSPSSLSASVGDRTTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNNRFGVPSPRFGSGSGTDFTLTISLQPEDFAFYCSQST
HVELTFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVYCLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYISLTITLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.51)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

MKKNIAFLIASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVKQAPGKLEWVGYIDPSNGETTYNQKFKGRFTLSDNSKNTAYLQMNSLRAEDTAVYY
CARDYRNGDMFEDWVGQGLTVVSSASTKGPSPVFLAPSSKSTSGGTAALGCLVKDYF
PEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVFPSSSLGIQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT (SEQ ID NO.55)

FIG. 31C

107250-95292160

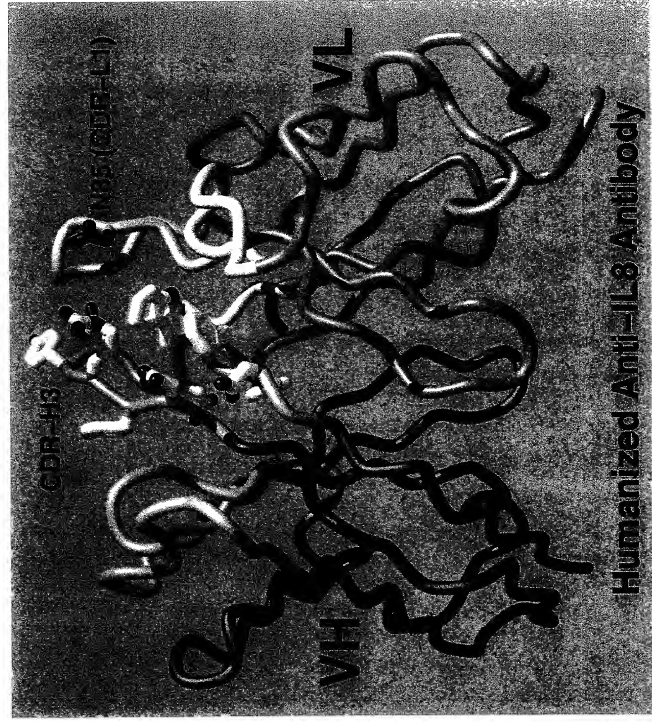


FIG. 32

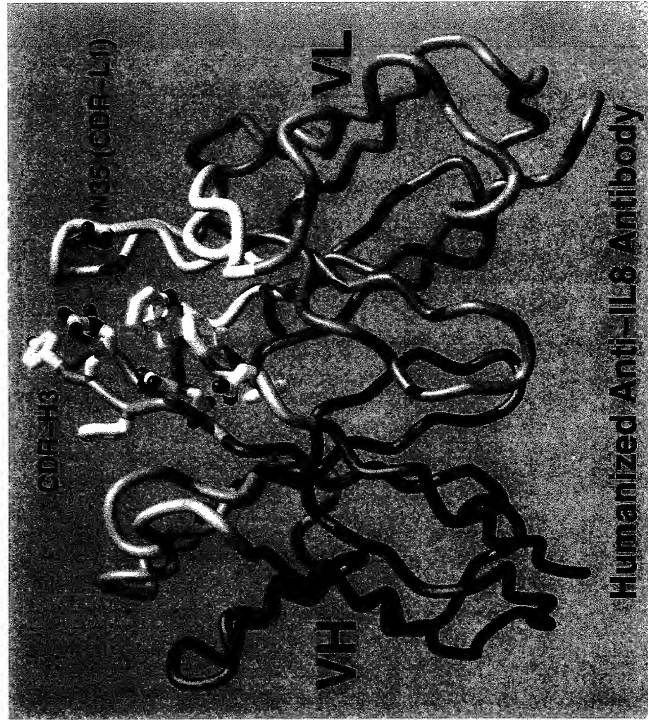


FIG. 32

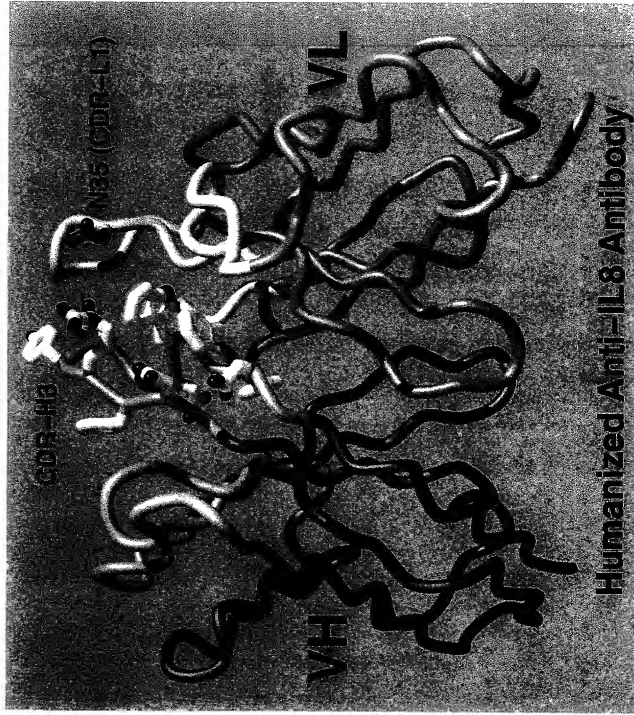
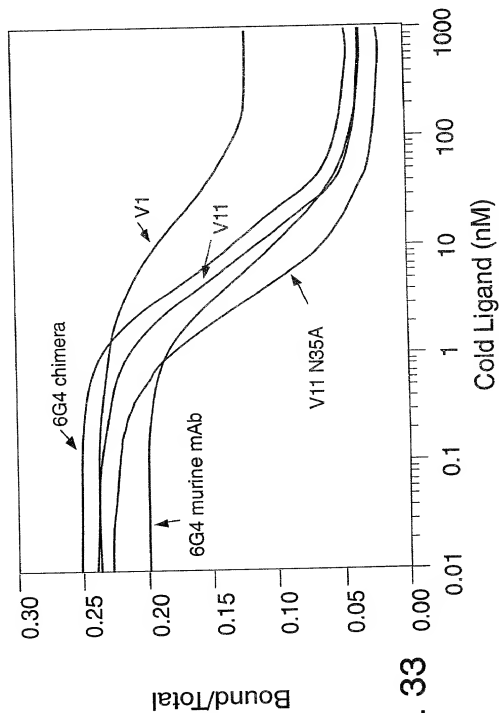


FIG. 32



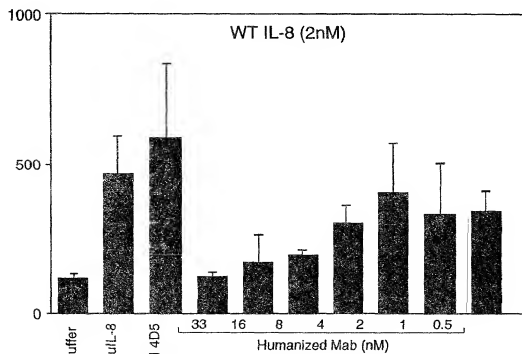


FIG. 34A

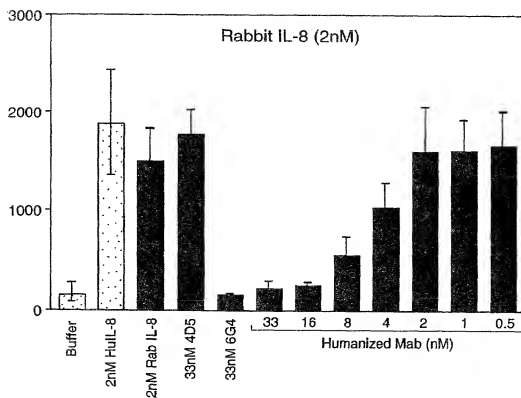


FIG. 34B

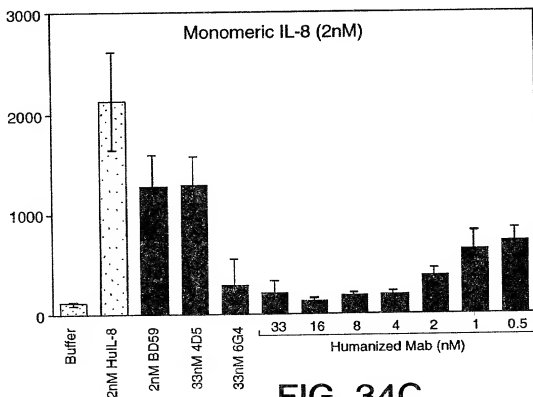


FIG. 34C

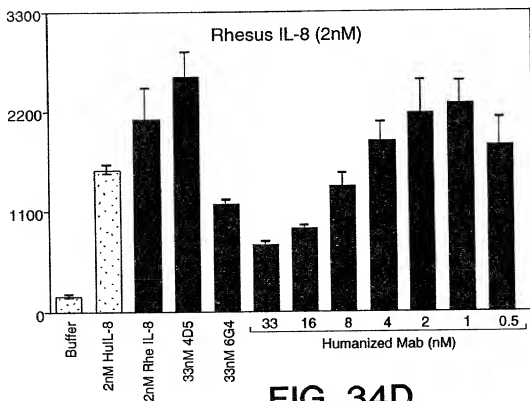


FIG. 34D

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTTITCRSSQSLVHGIGATY
LHWYQOKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCSQST
HVP¹LTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCILINNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO.56)

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGSLRLSCAASGYSFSSHYMH
WVRQAPGKLEWVG¹YIDPSNGETTNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRNGDWFDVWGQGLTVTVSSASTKGP²SVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVFSSSLGTQTYICNVN³HKPSTYK
VDKKVEPKSCDKTHT (SEQ ID NO.57)

Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPFCPAPELLGGRMKQLEDKVEELL⁴SKNYHLENEVARLKKLVGER (SEQ ID NO.57)

FIG. 35

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTG TTTTTCCTAT TGCTACAAAC
TACTTTTCTT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCCTC TGTGGGCGAT
CGTATCGGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT
TCCCACTGGT AGTCGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATCGTAA
18 R V T I T C R S S O S L V H G I G A T Y

181 TTACTCTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCCTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCTGT CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCCGCACTT ATTACTGTTT ACAGAGTACT
GATCGGTAGT CGTCGACGCT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCCG TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCTCTG TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGGAG ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCACTTT CCACCTATTG
138 V C L L N N F Y P R E A K V D S K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGAGGGTTA GCCCATTTGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCTGT CCGTGTCTGG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCTCTA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCTGTCTG TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGGCTT AGTGGGTAGT CCGGACTCG CCGGGGAGT GTTTCGTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G
(SEQ ID NO.58)

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGCCC CTAGTACGCA ACTAGTCGTA
CTCACAAATC GACTAGGAGA TCGGCCTTGC GTAGACCCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.56)

FIG. 36

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
TTTTCCCATG GATCTCCAAC TCCACTAAAA TACTTTTCTT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTTG TTTTTCCTAT TGCTACAAAC GCGTACGCTG AGGTTACGCT AGTGCACTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GCGGTTGGCC TGGTGCAGCC AGGGGGCTCA CTCGTTTGT CCGTGCAGC TTCTGGCTAC
CGCCACCCGG ACCACGTCCG TCCCCGAGT GAGGCAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG CGACTCCGGG GCCCATTCGC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
CAACCTATAT AACTGAAGAG GTTACCACTT TAGTTTTCAA TAGTTCCGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCCTTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTGCTATGG ACGTCTACTT GTCGAGCACA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
CGACTCCTGT GAGCGCAGAT AATGACACGT TCTCCCTTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCCTG GTCACCGTCT CCTCGGCCCTC CACCAAGGGC
AAGAAGCTGC AGACCCCACT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGA GACCCCGGTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCGGAA CCGGTGACGG TGTGCTGGA CTTAGCGGCC
CCGACGGACC AGTTCTGTAT GAAGGGGCTT GGCACCTGCC ACAGACCTTT GAGTCCCGGG
148 G C L K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
GACTGGTCGC CGCAGCTGTG GAAGGGCCGA CAGGATGTCA GGAGCTCTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCAGCAGC TTGGGACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTGCTCG AATCCGTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCAACAAG CCAGCAACAC CAAGGTGAC AAGAAAGTTG AGCCCAAACT TTGTGACAAA
TTAGTGTTCG GGTGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

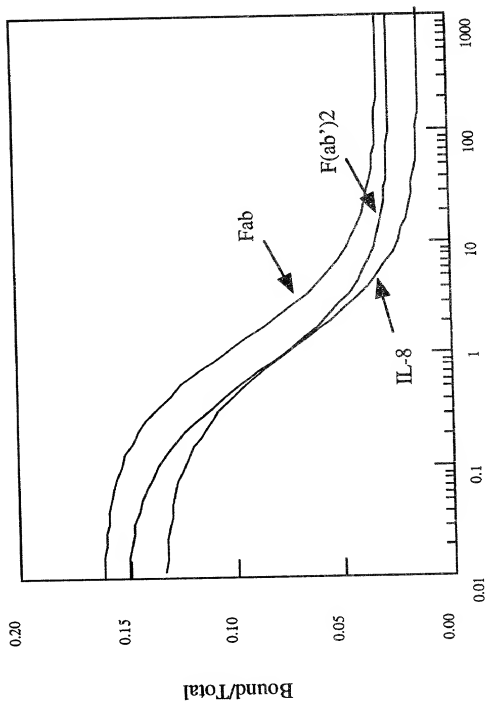
1561 ACTCACACAT GCCCGCCGTG CCCAGCACCA GAACTGCTGG CGGGCCGCAT GAAACAGCTA
TGAGTGTGTA CGGGCGGCAC GGGTCTGGT CTTGACGACC CGCCCGCGTA CTTTGTTCGAT
228 T H T C P P C P A P E L L G G R M K Q L

FIG. 37A

1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA
CTCCTGTTCC AGCTTCTCGA TGAGAGGTTT TTGATGGTGG ATCTCTTACT TCACCGTTCT
248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA (SEQ ID NO.59)
GAGTTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O (SEQ ID NO.60)

FIG. 37B



Cold Ligand (nM)

FIG. 38

FIG. 39

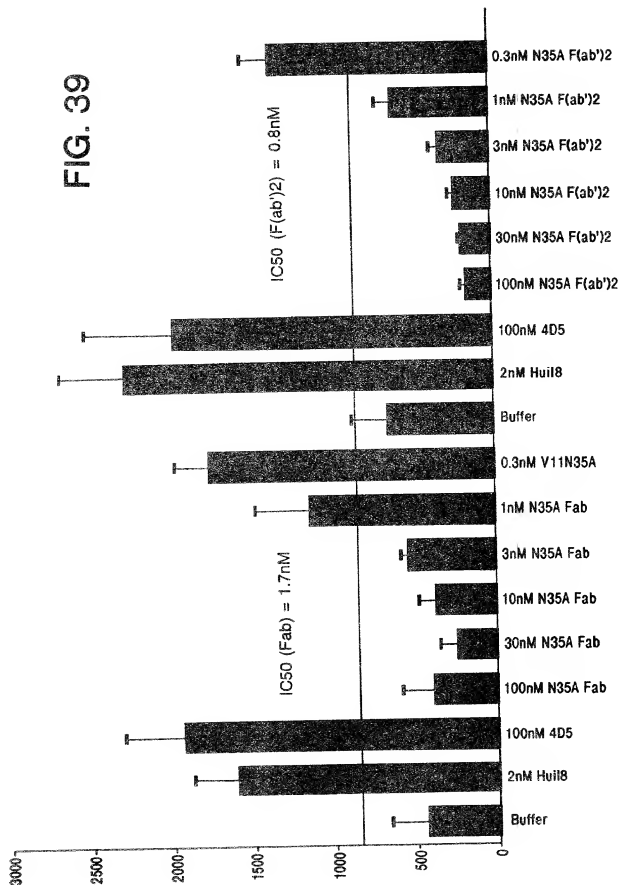
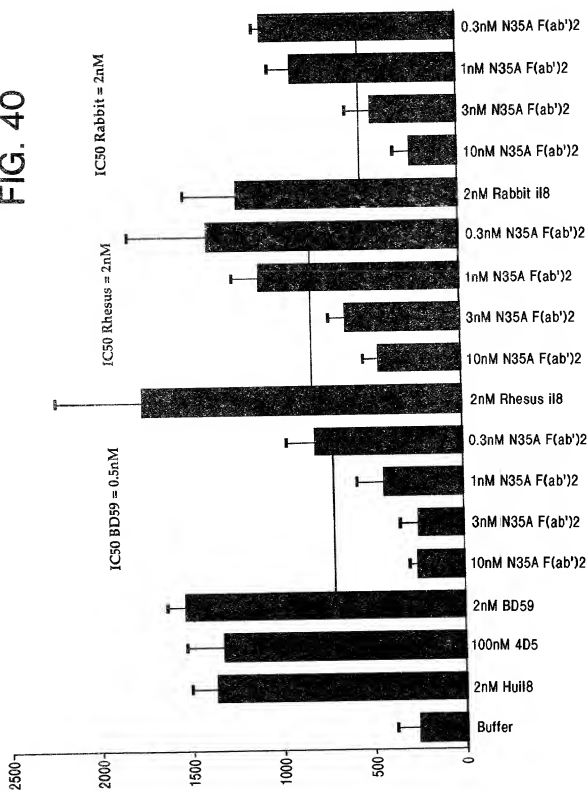


FIG. 40




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scrFI
ncII
nspI
hpaII
dsv
xmaI/pspAI
smaI
scrFI
ncII
dsv
cauII
bsaJI
avaI
sau3AI tagI
mboI/ndcII[dam-]
rseI
cep6I
nlaIV
kpaI cauII dpmI[dam-]
hgiCI bstYI/xhoII
banI bsaJI alwI[dam-]
asp718 bamHI auaI
acc65I alwI[dam-] mnlI mnlI
401 TCGGTACCG GGGATCGCT CGAGGTGTGAG GTGATTATTAT GAAGAAGAT ATCCGATTTC TTCTTGCATC TATGTTGCTT TTTTCTATTG CTCAAAAGC
AGCCATGGGC CCTAGGAGA GTTCAACTC CACTAAATA CTTTTCCTA TAGCGTAAG AGAGCTAG ATACAGCAA AAAAGATNAC GATGTTGCG
M K K N I A F L L A S M F V F S I A T N A
a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G toT ^

sstI
sacI
hgiJII
hgiAI/aspHI
ecII36II
bsp1286
bsiHKAII
bsmFI bsvI
barI auaI aluI
tthIII/aspI banII
ecorV
501 ATACGCTGAT ATCCAGATGA CCCAGTCCCC GAGCTCCGTC TCCTGCTGTC TGGGGATAG GGTCAACATC ACCTGGAGGT CAGTCAAG GTTAGACAT
TATCCGATCA TAGGTCTACT GGTCAAGGG CTGAGGAGC AGCGGAGAC ACCGCTATC CCAGTGTAG TGCAGTCCA GTTCGTTTC GAATCATGA
-2 Y A D I Q M T Q S P S S L S A S V G D R V T I T C R S S Q S L V H

```

FIG. 41B

```

601 GGTATAGAGTGC CTAAGTATTT AGCTGGATT CACACGAAC CAGGAAAGC TCGGAACTA CUGATTACA AAGTATCCAA TCGATTCTT CGAGTCCTT
CCATATCCAC GATGCATAAA TGTGACATA GTTCTTTG GTCCTTTG AGCTTTGAT GACTAATG L I Y K V S N R F S G V P S
32 G I G A T Y L H W Y Q Q K F G K A P K L L I Y K V S N R F S G V P S

berI
mspI
hpaII
bclI
bsaBI
sau3AI
mboI/ndeII[dam-]
dpuI[dam+]
dpuII[dam-]
alwI[dam-]
nlaIV
bstYI/xhoII
bamHI
alwI[dam-]
bsmFI
701 CTGGCTTCTG TGAATCGGT TCTGGAGCG ATTCACTCT GACCATCAGC AGCTGCGAGC CAGAGAGACT CGCACTTAT TACTTTTAC AGAGTACTCA
GAGCAGAGAG ACCTAGGCGA AGACCTGGC TAAGTGAGA CTGGTAGTG TCAGAGTCG GTCTTCTGAA CGCTTGATA ATGACAAGT TCTCATGAT
66 R F S G S G S G T D F T L T I S S L Q P E D F A T Y Y C S Q S T H

styI
bsaJI
rsal
csp6I
nlaIV
kpnI
hgiCI
bani
asp7I8
acc65I
msaII
bsrBI
acII
bsmFI
801 TGTCCGCTC AGCTTTGAC AGCTTTGAC GFTGAGATC AAACGAACTG TGGTCTGACC ATCTGCTTC ATCTCCCGC CAGTCGATCA CGAGTGTGAA
ACAGGGGAG TCCAAACGCTG TCCATAGCTT CCACCTCTAG TTTCCTGAC ACCAGCTGG TAGACAGAG TAGAAGGGG GTAGCTACT CTCACCTCT
99 V P L T F G Q G T K V E I K R T V A P S V F I F P P S D E Q L K

scriFI
mvaI
ecorII
dsav
bstNI
alwI
apvI[dam+]
601 GGTATAGAGTGC CTAAGTATTT AGCTGGATT CACACGAAC CAGGAAAGC TCGGAACTA CUGATTACA AAGTATCCAA TCGATTCTT CGAGTCCTT
CCATATCCAC GATGCATAAA TGTGACATA GTTCTTTG GTCCTTTG AGCTTTGAT GACTAATG L I Y K V S N R F S G V P S
32 G I G A T Y L H W Y Q Q K F G K A P K L L I Y K V S N R F S G V P S

tfII
hinFI
bsmFI
tagI
bpmI/gsuI[dam-]
claiI
bsp106
pleI
bspDI[dam-]
hinFI

```

FIG. 41C

FIG. 41D

-23

5-

scrFI
mval
scrFI

FIG. 41E

196

[illegible][illegible]

FIG. 41H

501
 GCGCGGCCA GTCTCTCTG CTTCCTACT TCGAGCACT ATCGACTAG CGATCATGGC GACACACCC GTTCCTGGA TCTCTACG CCGCTGGTAG
 GCGCGGGGT CAGGACACC GAGGACATG ACTCTGGTA TAGCTGATC CCTAGTACG CTGGTGTGG CAGGACACCT AGGAGATGGC GCGCTGGTAG

FIG. 41J

FIG. 41K

[illegible]

CGGGGTGCG TTATCTGTTA GCAGCATGTA TCACOGATAC GCGAGCGAAC GTGAAGCGAC TCGTCTGCAC maell ddeI nlatII
GCCCCACAGS ATAGCAACT CCGTCCTACT ATGGCTATG CGTCGGTGTC CACTTCGCTG AGCAGACGCI ITTGACGAGC CTGCACTGCT TGTGTGACT

3701

FIG. 41M

[illegible]

FIG. 41N

FIG. 410

[illegible]

[illegible]

FIG. 41Q

5201 TCTGCTGAG CCASTTACT TCGGAAGAAG AGTTGTAGAC TCTTGTATCG GCAACAACAC CACCGCTGGT TTTTTGTTTG CAGCAGCAG
 AGACACTTC GGTCAATGGA AGCCTTTTTC TCAACCATCG AGAATAGCG GTTGTGTTTG GTGCGAACCA TCGGCACCA AAAACAACAC GTTCGTGCTG
 eco57I bsrI maeIII
 sau3AI
 mboI/ndeII[dam-]
 hpaII
 sau3AI
 mboI/ndeII[dam-]
 dpnII[dam-]
 dpnII[dam-]
 aluI
 napBI
 acII
 caeII
 fnu4HI
 bsoFI
 bbvI
 5501 ATTGAGGCA GAAAAAGC ATTCACAGAA GATCCTTTGA TCTTTTCTAC GGGGTCTGAC GTCCAGTGA AGCAAACTC ACCTTAGGG ATTTTGCTCA
 TRAFGGGGT CTTTFTTTC TAGACTTCTT CTAGAACTCT AGAAAAGTG CCCAGACTG CAGACTCACT TCGTTTGG TGCATTTCCC TAAACCACT
 sau3AI
 mboI/ndeII[dam-]
 rnaI
 hphI
 dpnI[dam-]
 mboII[dam-]
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam-]
 dpnI[dam-]
 dpnII[dam-]
 dpnII[dam-]
 bstYI/xhoII
 bstYI/xhoII
 aluI/draI
 bfaI
 shaII/draI
 msei
 tru9I
 msei
 tru9I
 msei
 shaII/draI
 sau3AI
 mboI/ndeII[dam-]
 hpaII
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam-]
 dpnII[dam-]
 dpnII[dam-]
 bstYI/xhoII
 bstYI/xhoII
 aluI/draI
 bfaI
 shaII/draI
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 sau3AI
 mboI/ndeII[dam-]
 hpaII
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 dpnII[dam-]
 dpnII[dam-]
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 hpaII
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 mboI/ndeII[dam-]
 dpnI[dam-]
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 dpnII[dam-]
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 bstYI/xhoII
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 msei
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 hpaII
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam-]
 dpnII[dam-]
 dpnII[dam-]
 bstYI/xhoII
 bstYI/xhoII
 aluI/draI
 bfaI
 shaII/draI
 msei
 tru9I
 msei
 shaII/draI
 sau3AI
 mboI/ndeII[dam-]
 hpaII
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam-]
 dpnII[dam-]
 dpnII[dam-]
 bstYI/xhoII
 bstYI/xhoII
 aluI/draI
 bfaI
 shaII/draI
 msei
 tru9I
 msei
 shaII/draI
 sau3AI
 mboI/ndeII[dam-]
 hpaII
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam-]
 dpnII[dam-]<

FIG. 41B

[illegible]

FIG. 41S

[illegible]

FIG. 41T

[illegible]

FIG. 41U

```

>length: 6563

aatII(GACGTC): 1645 6489
acc65I(GGTACC): 403 823
accI(GTAKAC): 1093 1963 4449
accIII(TCCGGA): 3867(dam-)
actI(CGCG): 178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3357 3412
3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
see hinII

acyI
arIII(ACRGCT): 1307 4678
arIII(ACRGCT): 1788
ageI(ACCGGT): 1645 1813 2616 2637 2751 3408 6107 6489
ahaiI(bsaHI(GRCGTC): 5435 5454 6146
ahaiI(draI(TTNAKA): 346 5566
ahdI/eam1105I(GACNNNNCTG): 72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
alul(AGCT): 218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
5922
alw44I/snoI(GTGCAC): 1831 4494 4992 6238
alwI(dam-)(GGATC): 412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
alwNI(dcm-)(CAGNNNCTG): 1117 1385 5089
apaI(GGCGC): 1695
apaI/snoI(GTGCAC): 1831 4494 4992 6238
apoI(RAATT): 1 391 4093
apyI(dcm-)(CCGGG): 640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
aseI/asuI/vspI(ATTAAT): 5742
see asuI
asnI 905 930 4234 6166
asp700(GAANNNTTC): 403 823
asp718(GGTACC): see bglAI
aspiI see tbbIII
aspi 1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
asuI(GGNCC):

```

FIG. 41V

Stop Template Primer

SL.97.2 5' CAT GGT ATA GGT IAA ACT TAT TTA CAC 3' (SEQ ID NO.63)

NNS Randomization Primer

SL.97.3 5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3' (SEQ ID NO.64)

FIG. 42

Randomization of Position N35 of Variable Light Chain CDR-1
Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

Amino Acid	Frequency	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	6	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine	1	5.6	ND
Serine	1	1.9	ND

FIG. 43A

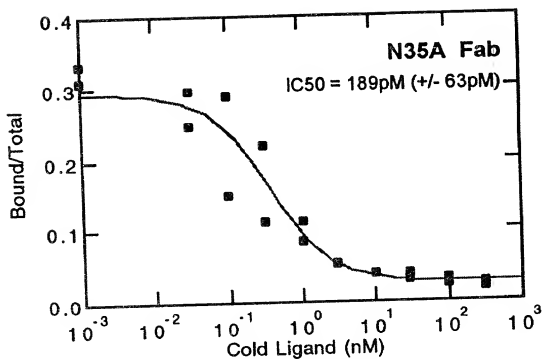


FIG. 43B

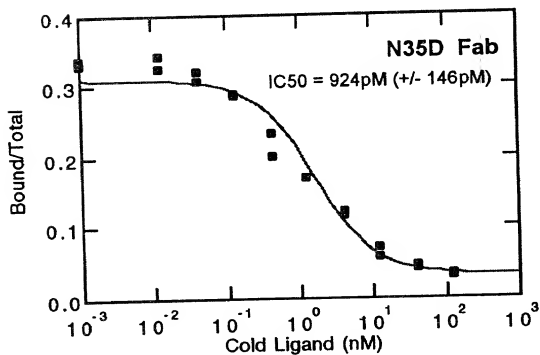


FIG. 43C

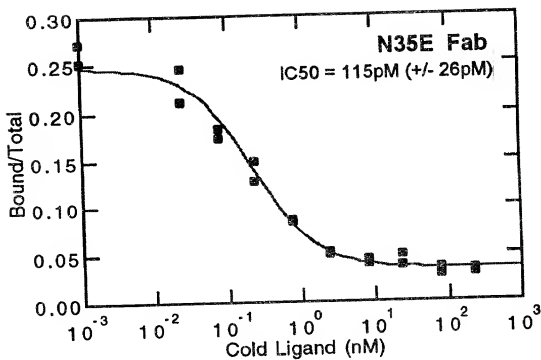


FIG. 43D

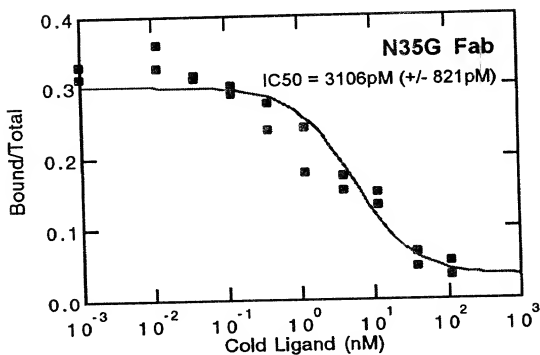
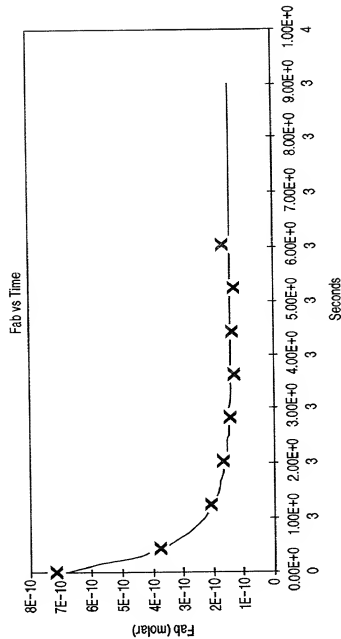


FIG. 43E



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')₂

SAMPLE	ka	kd	Kd
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') ₂	2.0x10 ⁶	2.1x10 ⁻⁴	109pM
6G4V11N35E-Fab	4.7x10 ⁶	2.6x10 ⁻⁴	54pM

FIG. 44

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTG TTTTTCATAT TGCTACAAAC
TACTTTTCTT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCGCCCTC TGTGGGCGAT
CGTATCGGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGCGCGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT
TCCCAGTGGT AGTGCACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACTCTGCATA
18 R V T I T C R S S O S L V H G I G E T Y

181 TTCACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGTAAAGA GACCTCAGGG AAGAGCGAAG AGACCTPAGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTT ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTCTTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S O S T

361 CATGTCGCCG TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGTCTT ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCCTG TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGGATAAC
CACACGGAGC ACTTATTGAA GATAGGGTCT CTCGGGTTTC ATGTCAACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCAATTGAG GGTCTCTCA CAGTGTCTCG TCTGTGCTGT CCGTGTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGACCCTT GACGCTGAGC AAAGCAGACT ACGAAGAAAC CAAAGTCTAC
ATGTGCGAGT CGTCGTGGGA CTGCGACTCG TTTCTGCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGACGCTTC AGTGGGTAGT CCGGAGCTCG AGCGGGCAGT GTTTCGTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G
(SEQ ID NO.65)

721 GAGTGTAAAG CTGATCTCTT ACGCCGGAGC CATCGTGCC CTAATACGCA ACTAGTCGTA
CTCAAAATTC GACTAGGAGA TGCGGCCCTG GTAGACCCGG GATCATGCGT TGATCAGCAT
218 E C O (SEQ ID NO.62)

FIG. 45

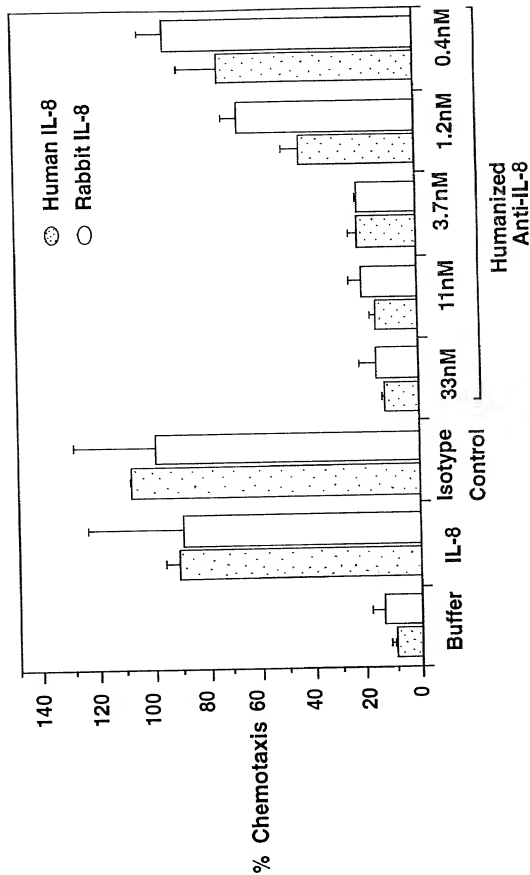


FIG. 46

N35AH1 upr

5-CTAGTGCAGCTGGCGGTGGCTGGCAGCCAGGGGGCTCACTCCGTTTGTCTGTGCAGCTTCTGGCTACTCCTTC-3'
(SEQ ID NO.66)

N35AH1 lwr

5-TCGAGAAGGAGTAGCCAGAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCGCCAGACTGCACT
(SEQ ID NO.67)

AG-3'

Bold indicates nucleotide change destroying PvuII site.

FIG. 47

> length: 8120 (circular)
 >This has the pSV1 backbone with the pRK7 cloning linker (pSV1) and the intron DHFR(1D)
 >made from pSV1.WTSD.D by adding a linearization linker(LL) into the HpaI site

```

cac8I
aluI
sacI
hgiI
hgiAI/aspHI
ecII36II
bapI286
bsiHMAI
bmyI
banII
tagI
1  TTGGAGTCCS CCCGACATG ATTATTGACT AGAGTGCTG GACACGTGTG GATGTGTGT CAGTTAGGT GTGGAAAGTC CCCAGGCTCC CAGAGGCA
   AACCTCGAGC GGGCTGTAC TATTAAGTCA TATCACTGAT CTCGTGACAC CTTCACACA CTCACATCCA CACCTTCAG GGGTCCGAG GGTCTCCGT
   scfI
   sfanI
   ppulOI
   nsiI/avaII
   nlaIII
   sphi
   nepI
   nspII
   cac8I
   cse8I
   101 GAGATATCC AAGAGTCAT CTCATATGAT CAGCAGCAG GTGTGNAAG TCCCTAGGT CCCGACAGG CAGAGATATG CAAAGCATGC ACTCTAGTA
   CTCATAGCT TTCTACATCA GAGTAAATCA GTGTGTGTC CACACCTTC AAGGTGCTCA GGGTGTGTC GTTCTATCA GTTCTGACG TTAGTATAT
   nlaIII
   styI
   ncoI
   bclI
   dsal
   acII
   acII foki
   bsmFI
   201 GTGAGACAC ATAGTCCGC CCTTAATCC CCCCATCCS CCCCTAATC CCCGCTTC GCGCCATTCT CGGCCCATG CGCGCCATG TTTTITAT
   CAGCTGTTC TTTACAGGCG GGGATTGAG CGGTAGGC CGGTAGGC GGGATTGAG GCGGTACAG GCGGTAGAG GCGGGGTAC CGACTGATTA AAAAATTTA

```

FIG. 48A

[illegible]

FIG. 48B

601 CAGAGATGCA GCGACACTC TTACGTGGAA GGTAAACAGA ATCTGTGAT TATGGGTGAG AATACCTGT TCTCCATCC TGACAGAT CGACCTTTA
 GTTCTTNCI GTGTGTGAG AATCACTTC CCATTGTCT TAGACCACTA ATACCATCC TTTCGACA ACAGGTGAG ACCTCTCTTA GTGTGAT

601 AGACAGAT TATNAGTT CTACGTAGAG AACTCAAGA ACCACACGA GAGCTCANT TTCTTGCCTA AGCTTGAT GATCCTTAA GACTTATGA
 TCTGTCTTA ATATACGA GACTCACTC TTGAGTTCT TGTGTGTCT CCGAGTNA AAGAGGCTT TTCAAACCTA CTACGGANT CTGAATACT

801 ACACACGGAA TTGCGACATA AGTAGACAT GGTGTGATA GTCCGAGCA GTTCTGTTA GTCCGAGCC ATGATCAAC CAGCGCACT TAGACTCTT
 TGTGGGCTT AACGTTAT TTCACTCTGA CGAACCAT CAGCTCTCT CAGACAAAT CAGCTCTGG TACTTGTG GTCCGTGGA ATCTGAGAA

601 CAGAGATGCA GCGACACTC TTACGTGGAA GGTAAACAGA ATCTGTGAT TATGGGTGAG AATACCTGT TCTCCATCC TGACAGAT CGACCTTTA
 GTTCTTNCI GTGTGTGAG AATCACTTC CCATTGTCT TAGACCACTA ATACCATCC TTTCGACA ACAGGTGAG ACCTCTCTTA GTGTGAT

601 AGACAGAT TATNAGTT CTACGTAGAG AACTCAAGA ACCACACGA GAGCTCANT TTCTTGCCTA AGCTTGAT GATCCTTAA GACTTATGA
 TCTGTCTTA ATATACGA GACTCACTC TTGAGTTCT TGTGTGTCT CCGAGTNA AAGAGGCTT TTCAAACCTA CTACGGANT CTGAATACT

801 ACACACGGAA TTGCGACATA AGTAGACAT GGTGTGATA GTCCGAGCA GTTCTGTTA GTCCGAGCC ATGATCAAC CAGCGCACT TAGACTCTT
 TGTGGGCTT AACGTTAT TTCACTCTGA CGAACCAT CAGCTCTCT CAGACAAAT CAGCTCTGG TACTTGTG GTCCGTGGA ATCTGAGAA

FIG. 48C

[illegible]

FIG. 48G


```

scrfi
ncll
mepi
hpalI
dsavI
cauli
xmal/pspal
smai
scrfi mval
ncll ecorII
dsav
cauli
foki
real
cspl
bep14071/bep321
aval
2401 CAGCCCCGAG AACACACAGT GTCACCCCTG CCCACATCCC GGGAGAGGAT GACCAAGAGC CAGGTACGCC TGACCTGGCT GGTCCAGGCC TTCTATCCCA
347 Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S
381 D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S
2501 GCGACATGCC GTGGGAGTGG GAGAGCAATG GCGAGCCGGA GACACACTAC AAGACACGCC CTCCCTGCTC GGACTCCGAC GCTCTCTCTC TCCTCTCAG
381 D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S
2601 CAGCTTACC GTGGACAGA GAGGTGGCA GCGAGGGAAC GTCTCTCAT GTCCCTGAT GCATCGAT CTGCACACCC ACTACACGCA GAGAGCCCTC
414 K L I V D K S R W Q G N V F S C S V M H E A L H N H Y T Q K S L

```

FIG. 48I

```

sau96I          acII haeIII/palI
                fnu4HI asuI
                bsoFI nlaII
                sfil styI          aluI
                eaeI ncoI          fnu4HI
                cfri dsai          bsoFI
                aluI haeIII/palI    bsvI          maeII
                hindIII bgII bsuI
2701 TCCTGTCTC CGSSTAATG AGTGGACAGG CCGTAGAGTC GAGCTGAGAG AGCTTGGCGG CGATGGGCCA ACTCTTTAT TGCAGCTTAT ATGCTGTAGA
AGGACAGAG GCCATTATAC TCAGCTGTCT CGCATCTGAG CTGAGCTGCT TGGACCGGCC GGTACCGGGT TGAACRAATA AGCTGATAA TTACCAATGT
447 S L S P G K O (SEQ ID NO:11)

                rmaI
                maeI
                bsmI bfaI
2801 AATTAAGCAA TAGCAACACA AATTTACAAA ATAAAGCAT TTTTTCATG CATTCATGTT GTGGTTTTC CAATCATATC AATGATCTTT AATCTCTG
TTATTTCTGT ATCTGATGCT TTAATGCTTT TATTTGTGTA AAAAATGATC GTAATGATCAA CACCAAAAGC GTTTGAGTAG TTACNTNGAA TATGACAGC
                rmaI
                maeI
                bsmI bfaI
                rsal
                cep6I
                nlaIV
                kpnI
                hgiCI
                banI
                mnlI
                asp718
                acc63I ddeI acII
2901 GATCATGCGG GATATATTC GCGGAGGAC CATGGCTGTA AATACTCTT GAAAGAGAA CTGTGGTAGG TACCTCTTGA GCGGGAAGA ACCATCTGTG
CTAGCTAGCC CTTAATTAG CCGGCTCTG GTACCGAGCT TTATTGAGA CTTTCTCTT GTAACCAATCC ATGGAAGACT CCGGCTTTCT TGTAGACAC

```

FIG. 48J

[illegible]

FIG. 48L

FIG. 48N

[illegible]

218 E C O (SEO ID NO.72)

sau3AI
 mboI/ndeII[dam-]
 dpaI[dam+]
 dpaII[dam-]
 pvuI//bspCI
 mcrI
 bsiEI
 taqI[dam-]
 clai//bsp106[dam-]
 bepDI[dam-] tru9I
 sau3AI msei
 mboI/ndeII[dam-]
 dpaII[dam+] xnnI
 dpaII[dam-] asei/aenI/vspi
 nlaIII alwI[dam-] asp700
 hhal/cfoI nlaIII
 4401 TTTTTCACGT GAAAGTATG ATCATGCTG GATCGATCG GAATTAATTC GCGGAGAC CAGTGGCGA
 AAAAAGTGAC GTAAGATCA CACCAACAC GTTGAGTAG ITACATAGAA TACTACAGAC CTATATTAAG CCGGCTGTG GTACCGAGT
 *sv40 origin

raeI
 cap6I
 nlaIV
 KpnI
 HgiCI
 bam718
 asc65Y ddeI acII
 mnlI
 mnlI
 4501 ATATACCTGT GAAGAGGAA CTGGGTATG TACTCTTGA GCGGGAAGA AACAGCTGT GAACTGTGT CAGTAGGCT GTGGAAAGTC CCGAGCTGC
 TTATTGGAGA CTTCCTCTT GACACATCC ATGGAGACT CCGCTTCT TGTGTGACAC CTATACACA STGATGCCA CACCTTTCAG GGGTGTCC

scaFI
 ppu10I
 nsiI/avaII
 nlaIII
 sphi
 nspi
 nspi
 nspi
 cac8I
 4601 CCACACAGA GAAGTATGCA AACCTGCTT CTCAATTAGT CAGCAACAG GTGTGAAG TCCTCAGCT CCGCAGCT CCGCAGCAG CAGAGTAGT CAAAGCTGC
 GTGTGTCTGT CTTCATAGT TTCTGACGA GATTAATCA GTGTGTGTC CAGACTTTC AGGGTCCGA GGGGTGTCTC GTTCTATAC GTTCTGTAG

FIG. 48P

[illegible]

FIG. 48Q

[illegible]

FIG. 48R

[illegible]

FIG. 48S

[illegible]

FIG. 48T

FIG. 48U

[illegible]

sau3AI mboI[dam-] theI fnuDII[mvn] cac8I
 sau3AI mboI[ndeII[dam-] fnuDII[mvn] cac8I
 dpmI[dam+] dpmI[dam+] fnu4HI
 dpmI[dam+] dpmI[dam+] fnu4HI
 bsvI[choII] alwI[dam-] hlnPI bsvI
 bsvI[choII] alwI[dam-] hlnPI bsvI
 hlnPI[choII] bsvI[choII] hlnPI[choII] bsvI[choII]
 alwI[dam-] bsvI[choII] hlnPI[choII] bsvI[choII]
 7101 TCAAGGATC TTCTTGATG CTTTCTTTC TGGCGGTAT CTTCTCTG GACACAAA AACACGCT ACCAGCGGTG GTTGTCTTC CGGATCAGA
 AGTTTCCTAG AAGACTCTA GGAAMAAAG ACCGCCATTA GACGACGAC GTTGTCTTC TGGTGGCGA TGGTGGCGA CTTTGGCGA CTTTGGCGA GCTAGTCTT
 xmaI maeI haeII[paI] haeI
 7201 GCTACACT CTTTTCGGA AGGTAACCTG CTTACGAGA GGGGAGATC CAACTACTG CTTCTAGT TAGCGCATC ATCGCATC ATCGCATC GAAGTCTG
 GATGCTG GAAAGAGCT TCAATTCACC GAATGCTCT CCGTCTATG GTTATGACA GGAATGACA ATCGCATC ATCGCATC ATCGCATC GAAGTCTG
 fnu4HI bsoFI bsvI fnu4HI
 bsoFI bsvI fnu4HI
 alwI[dam-] bsvI bsoFI
 bsvI bsoFI fnu4HI
 maeIII bsvI bsvI
 7301 TCTGTAGC GCGCTACATA CTTGCTG CTAATCTGT TACAGTGGT TCTGCTGCT TGGATGCT GCGATGCT CTTGTCTTAC CCGTGGGAC TCAAGAGAT
 AGCATCTG GCGATGCT GAGCGAGAC GATTGAGCA ATGCTACCG ACAGCTCA CCGTATCA GCAGAGAT GCCACCTG AGTCTGCTA
 acII hglAI/aspHI
 napBII fnu4HI bsp1286 bsiHKAI bsvI
 mspI bsvI bsvI bsvI
 bsaMI hlnPI bseII
 maeIII hlnPI/foI alw44I/snoI aluI
 7401 AGTACCGGA TTAGCGGAC GCGTGGGCT GAGCGGGG TGGTGACA CAGCCAGCT TGGAGCGAC GACCTACAC GACTGAGT ACCTGAGC
 TCAATGCT ATTCCGCT GAGGCCGA CTTGCCCGC AAGACGCT GTGCGTGA ACCTGCTG CTGGATCTG CTGATCTA TGGATCTG

FIG. 48W

scrFI mval
ecorII dsav
bstNI bseNI
bsseI hinfI mnlI
hhaI/cfoI aluI apyI[dm+]

7501 TGACGATTGA GAAAGCCCA CCGTTCGGA AGGAGAAAG GGGGAGAGT ATCCGGTAG CGGACGGTC GGAACAGGAG AGCCAGAGG GAGGTTCCA
CTCGTAACT CTTCGGGGT CGGAAGGGT TCCTCTTTTC CGCTCTTCCA TACGCAATC GGGTCCAG CTTGTGCTC CTGGAAGT

scrFI mval
ecorII dsav
bstNI bseNI
bsseI hinfI mnlI
hhaI/cfoI aluI apyI[dm+]

7601 GCGCGAAGC CGTGGATCT TTATAGTCT GTGCGGTTT GCGACTCTG ACTGAGGCT GATCTTCT GATGCTGTC AGGGGGGGG AGCTATGGA
CCCTTTGC GGACCATAGA ATATCAGGA CGTCCAGAG CCGTCCAGAC TGAATCCGA CTAATAACA CTAGAGCAG TCCCCCGCC TCGGATAGT

scrFI mval
ecorII dsav
bstNI bseNI
bsseI hinfI mnlI
hhaI/cfoI aluI apyI[dm+]

7701 AAACGCCAG CAGCGGGC TTTTAAAGT TCGTGGCTT TCGTGGCTT TCGTGGCTT TCGTGGCTT TCGTGGCTT TCGTGGCTT TCGTGGCTT
TTTTCGGCT GTTGGCGGG AAGATCCCA AGGACCGGA AACGACCGA AAGAGTGT AAGAGTAGG ACGCATAGG GGAATAGAC ACCTATTGC

scrFI mval
ecorII dsav
bstNI bseNI
bsseI hinfI mnlI
hhaI/cfoI aluI apyI[dm+]

7801 TTTTACCGG TTTGATGAG CTGATACCG TCGCGCAGC CGAACAGCC GTGCTGAGG GAGGAGCGG AAGAGCCGC AATAGCAAA
AATAGCGGG AACTCACTC GACTATGGG AGCGGGCG CCGTTCGCT CAGTCTGCT CTTCTGGC TTCTGGCG TTATGGGTT

FIG. 48X

[illegible]

FIG. 48Y

```

tru9I
msel
asei/asmI/vspt
xmi
nlaIII asp700
8101 TGACCATGAT TAGCATTIRA (SEQ ID NO.68)
ACTGGTACTA ATGCTTAAAT
>length: 8120

1690 5947
aatII(GAGGTC): 2659 3967 4529
acc65I(GGTAC): 823 1039 2738 4237
accI(GTMKAC): 217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
acII(CCGC): 3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3948 4031 4318 4542 4727
2139 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248
5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804
7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070
786 hmlI
acyI
efIII/bfr:(CTTAG): 932 7758
afIII:(ACRYGT): 1833
ageI(ACCGGT): 988 1690 1858 5117 5947 6329
ahaiI/bsaiI(GRCGTC): 696 4915 6290 6982 7001
ahaiI/drai(TTTAA): 696 2087 6865
ahdi/asmI105I(GACNNNGNC): 514 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340
alul(AGCT): 3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4954 5047 5333 5590
5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096
alw44I/enoI(CTGCAC): 1876 5651 6198 7444

```

FIG. 48Z

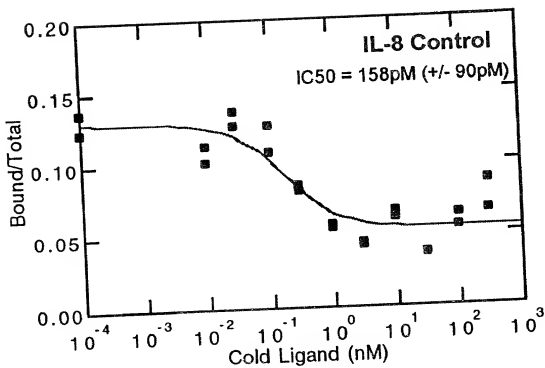


FIG. 49A

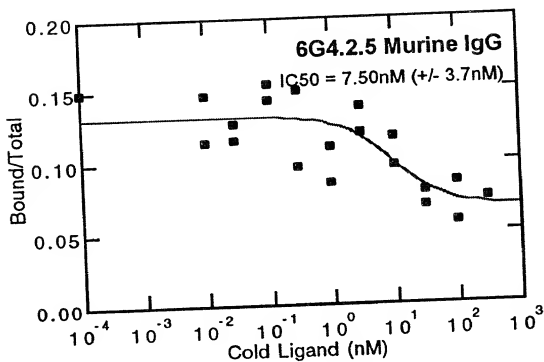


FIG. 49B

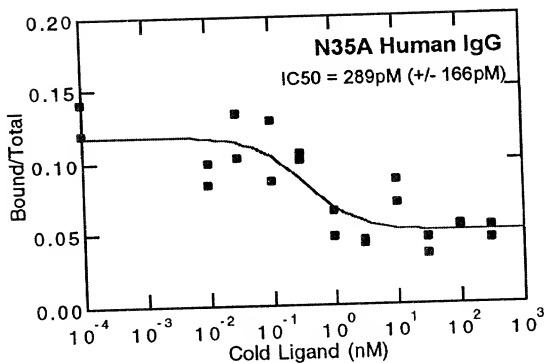


FIG. 49C

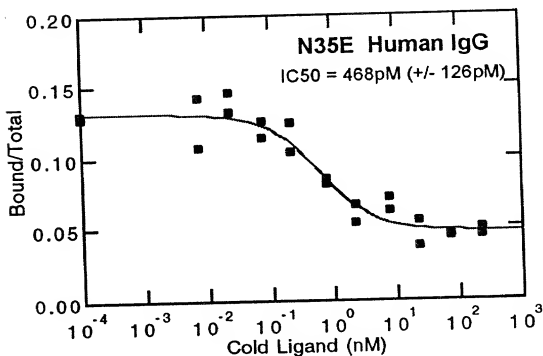


FIG. 49D

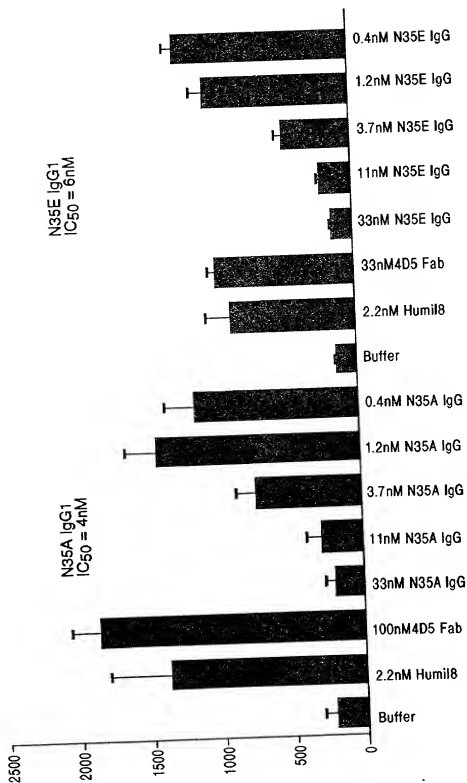


FIG. 50A

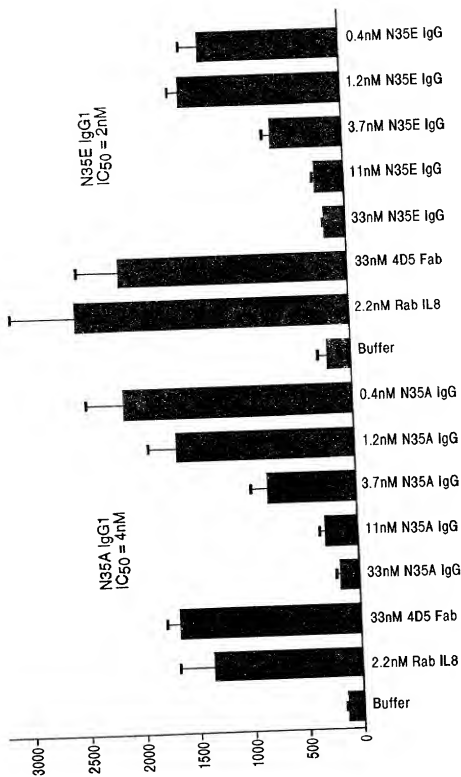
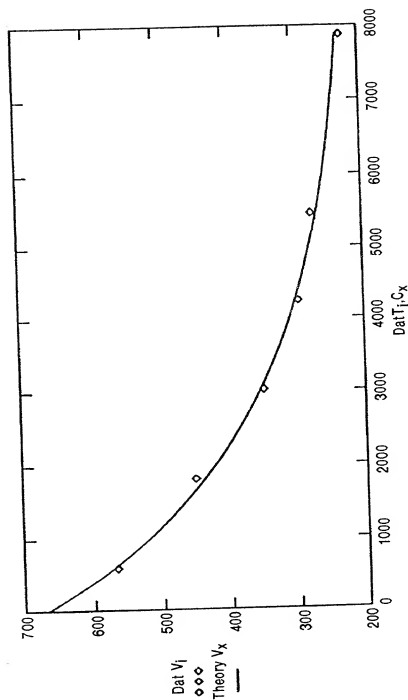


FIG. 50B



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A-IgG1

SAMPLE	ka	kd	Kd
Murine 6G4.2.5 IgG2a	8.3×10^5	2.9×10^{-4}	350pM
6G4V11N35A-IgG1	8.7×10^5	7.7×10^{-5}	88pM
6G4V11N35E-IgG1	3.0×10^6	1.4×10^{-4}	49pM

FIG. 51

10150-8222-46

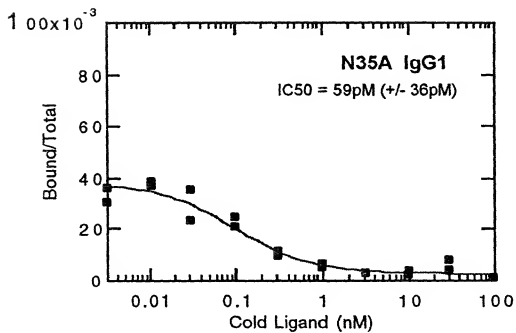


FIG. 52A

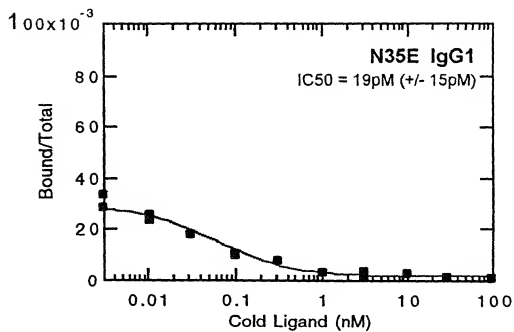


FIG. 52B

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
 TTTTCCCAT A GATCTCCAAC TCCACTAAAA TACTTTTTCT TATAGCGTAA AGAAGAACGT
 -1 M K K N I A F L L A

841 TCTATGTTG TTTTTTCTAT TGCTACAAAC GCGTACGCTG AGGTTCAGCT AGTGCAGTCT
 AGATACAAAG AAAAAAGATA ACGATGTTTG CGCATGCCAC TCCAAGTCCA TCACGTCAGA
 -11 S M F V F S I A T N A Y A E V Q L V Q S

901 GCGCGTGGCC TGGTGCAGCC AGGGGGCTCA CTCGGTTTGT CCTGTGCAGC TTCTGGCTAC
 CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAAACA GGACACGTCG AAGACCGGATG
 8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCATATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
 AGGAAGAGCT CAGTGATATA CGTGACCAG CGATCCGGG GCCATTCCC GGACCTTACC
 28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGCGCGT
 CAACCTATAT AACTAGGAAG GTTACCACCT TGATGCATAT TAGTTTTCAT GTTCCCGGCA
 48 V G Y I D P S N G E T T Y N Q K F K G R

1081 TTCACCTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTCGGT
 AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTGCTATGG ACGTCTACTT GTCGGACGCA
 68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCGCTCTA TTA CTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
 CGACTCTCTG GACGCGAGAT AATGACACGT TCTCCCTTAA TAGCGATGTT ACCACTGACC
 88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGAGC TCTGGGGTCA AGGAACCCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
 AAGAAGCTGC AGACCCCGAG TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
 108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCTCTC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
 GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGGTG TCGCCGGGAC
 128 P S V P L A P S S K S T S G G T A A L

1321 GCGTGCCTGG TCAAGGACTA CTTCCTCCGAA CCGGTGACGG TGTCTGTGAA CTCAGGCGCC
 CCGACGGACC AGTTCTCTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
 148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCTCGGCT GTCCCTACAGT CCTCAGGACT CTACTCCCTC
 GACTGGTCCG CGCACGTGTG GAAGGCGCGA CAGGATGTCA GAGTCTCTGA GATGAGGGAG
 168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCACGACGC TTGGGCAACC AGACCTACAT CTGCAACGTG
 TCGTCGCACC ACTGGCACGG GAGGTTCGTG AACCCGTGGG TCTGGATGTA GAGGTTGCAC
 188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTGCAC AAGAAAATTG AGCCCAATC TTGTGACAAA
 TTGCTGTTGG GGTCTGTGTG GTTCTTCAAC TCGGGTTTAG AACACTGTTT
 208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCCCGCCGTGA (SEQ ID NO.69)
 TGAGTGTGTA CGGGCGGCAT
 228 T H T C P P O (SEQ ID NO.70)

FIG. 53

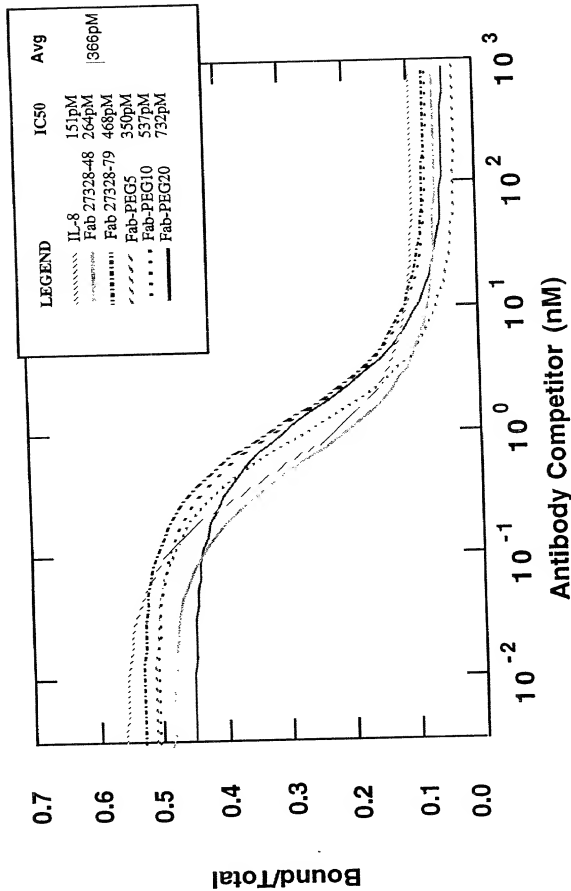


FIG. 54A

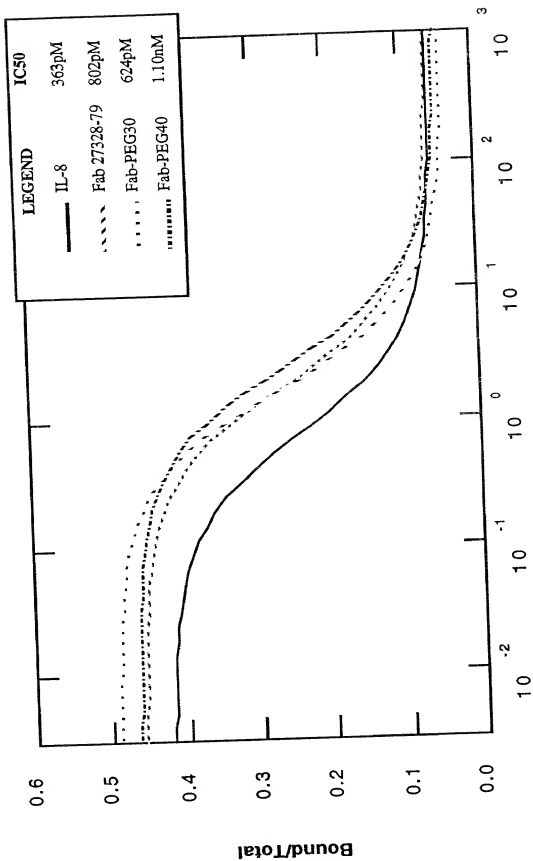
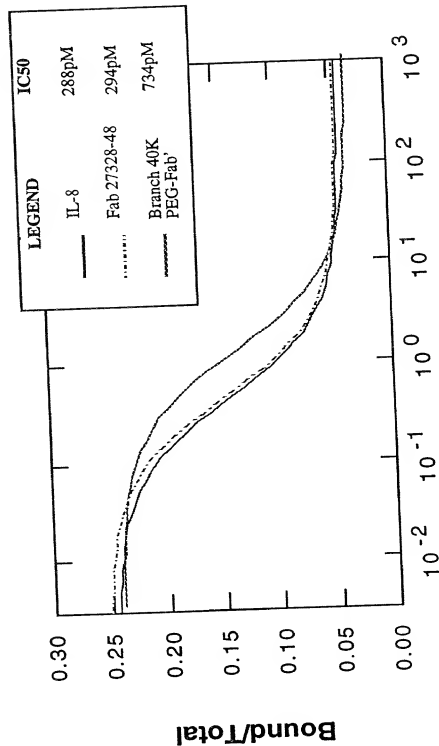


FIG. 54B



Antibody Competitor (nM)

FIG. 54C

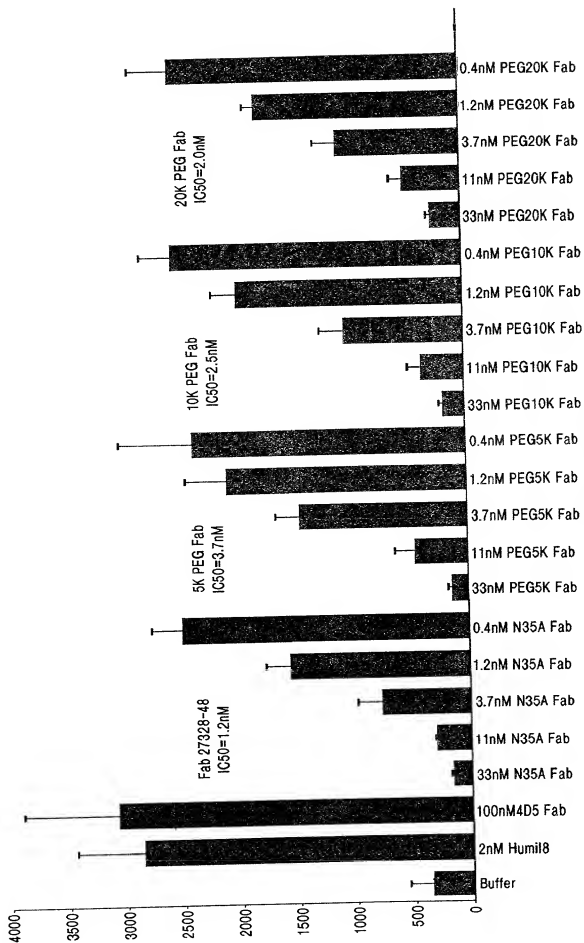


FIG. 55A

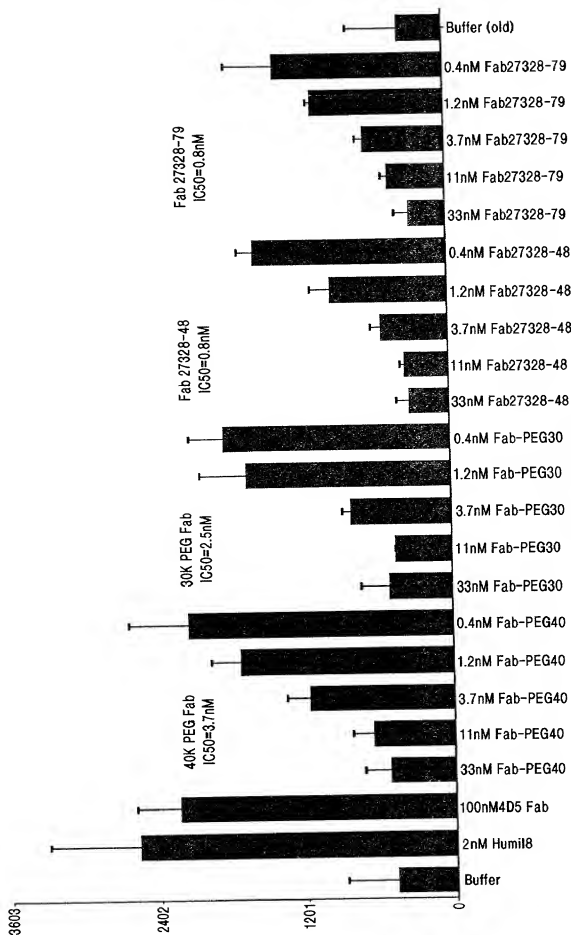


FIG. 55B

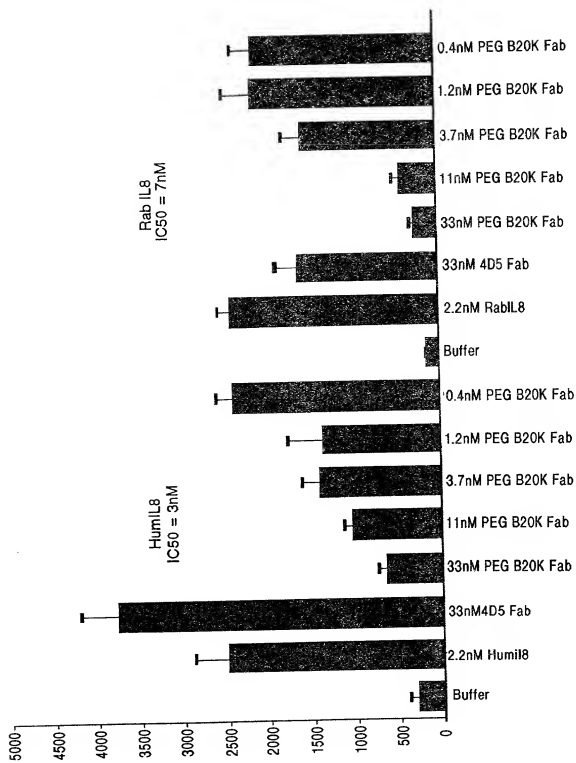
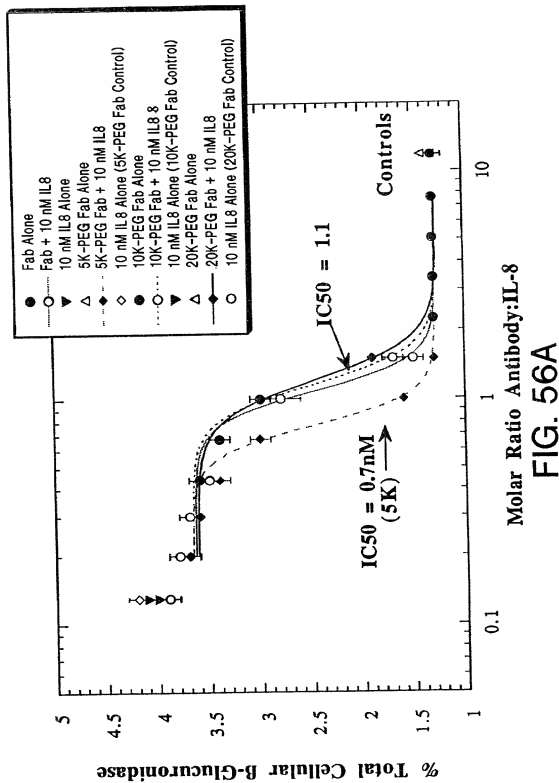
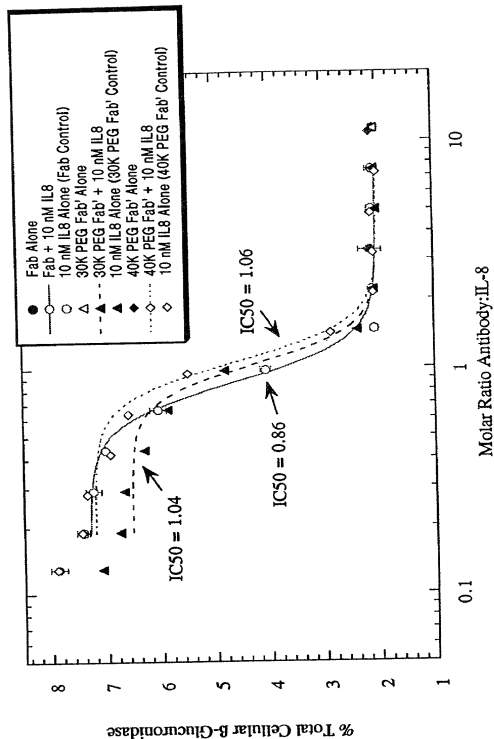


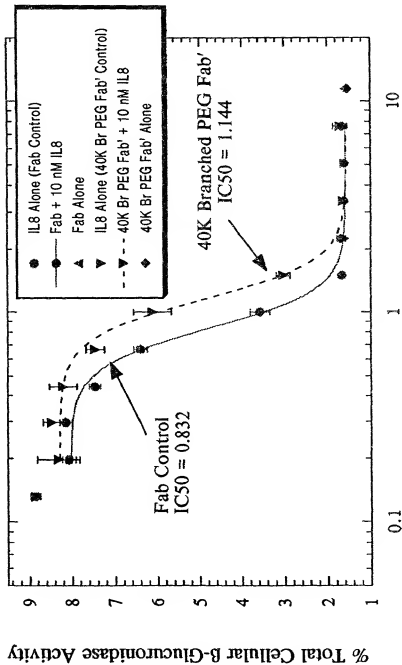
FIG. 55C





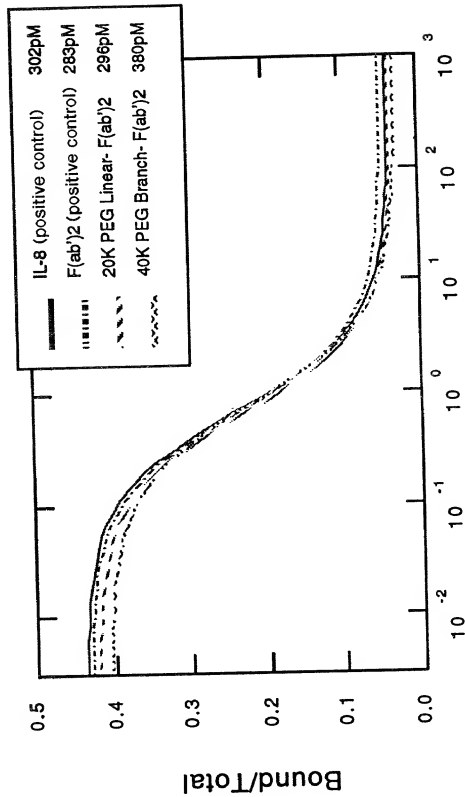
Molar Ratio Antibody:IL-8

FIG. 56B



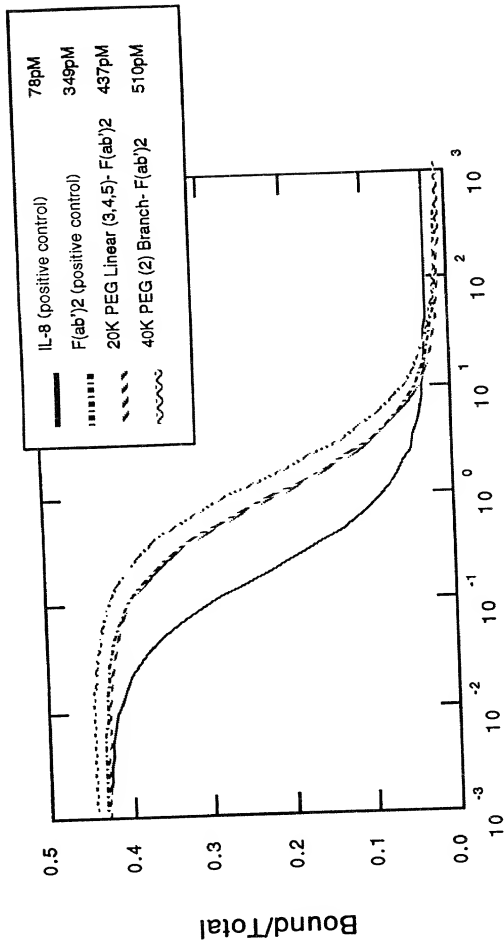
Molar Ratio Antibody:IL8

FIG. 56C



Pegylated F(ab')₂ (nM)

FIG. 57A



Pegylated F(ab')₂ (nM)

FIG. 57B

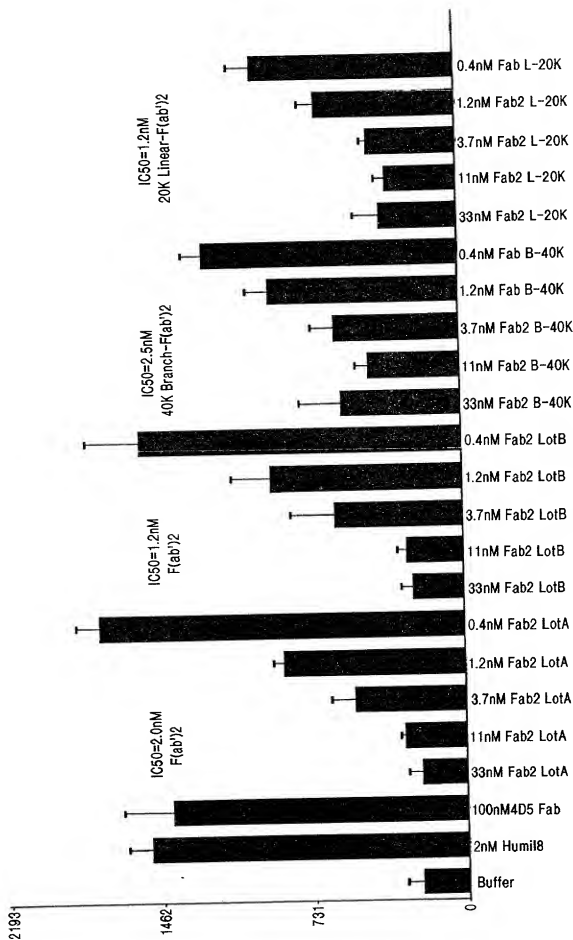


FIG. 58A

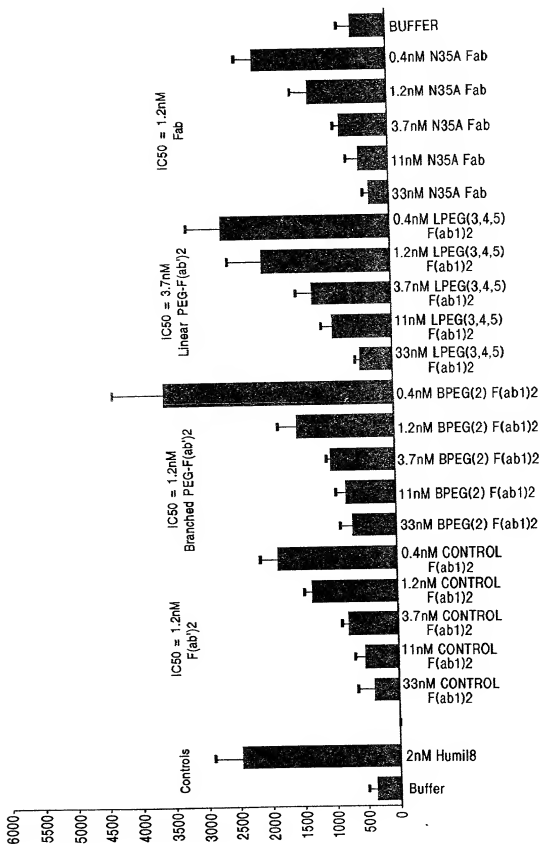


FIG. 58B

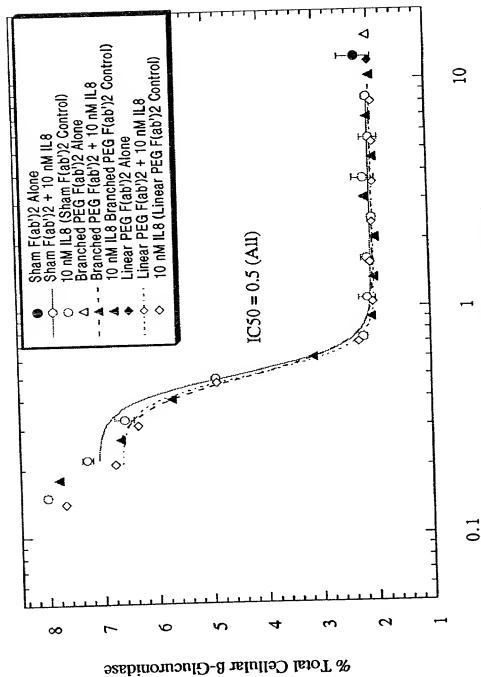
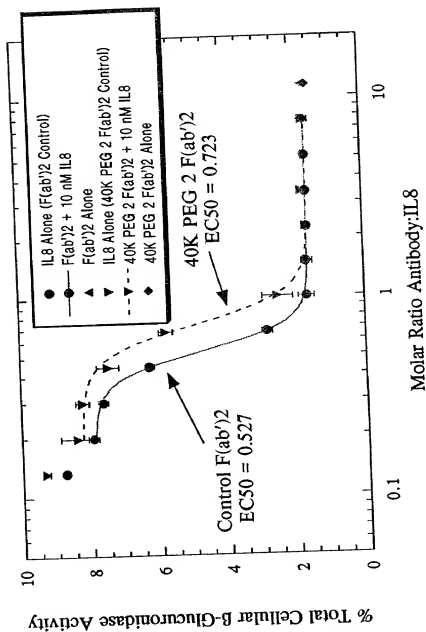
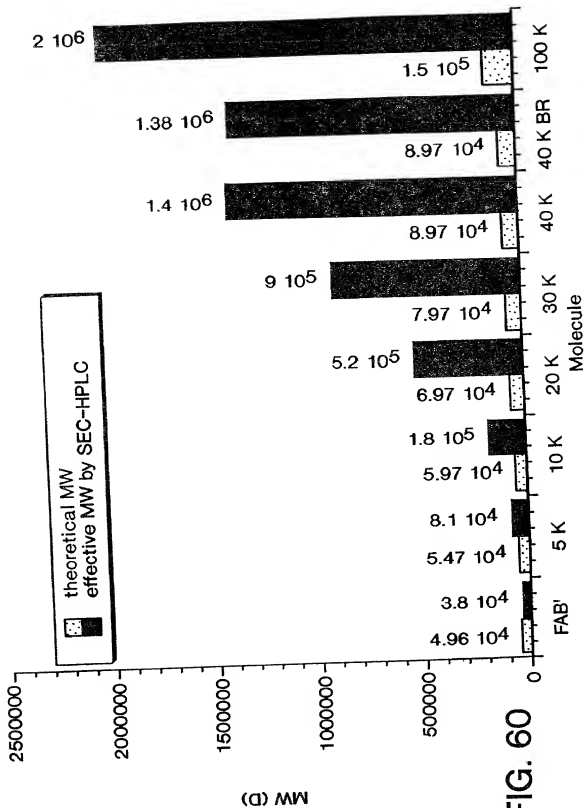
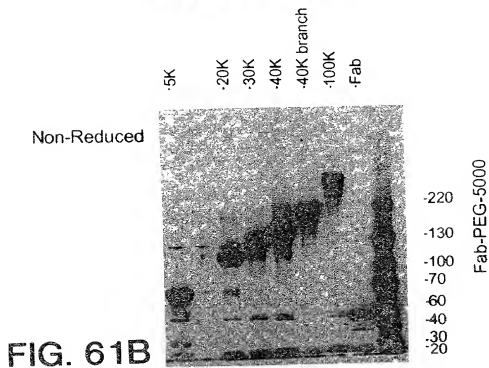
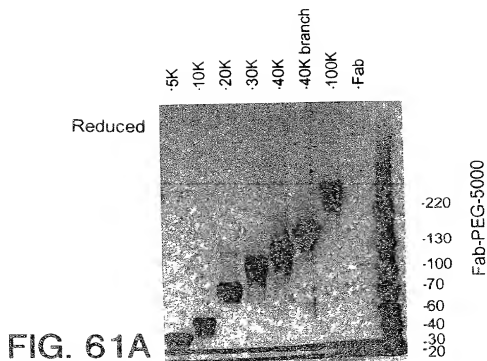


FIG. 59A







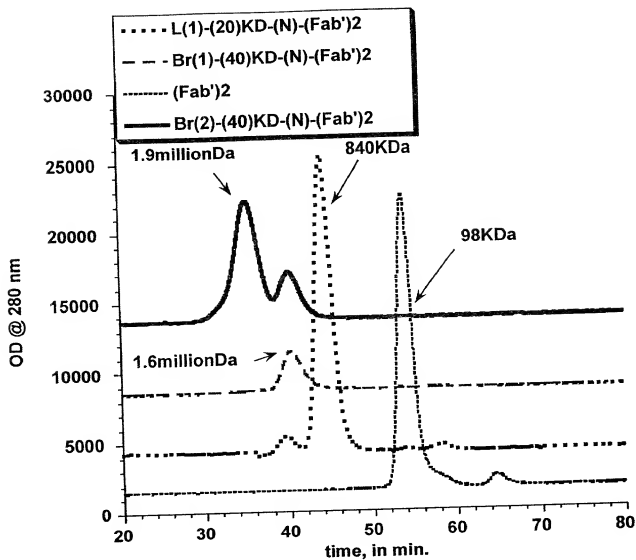


FIG. 62

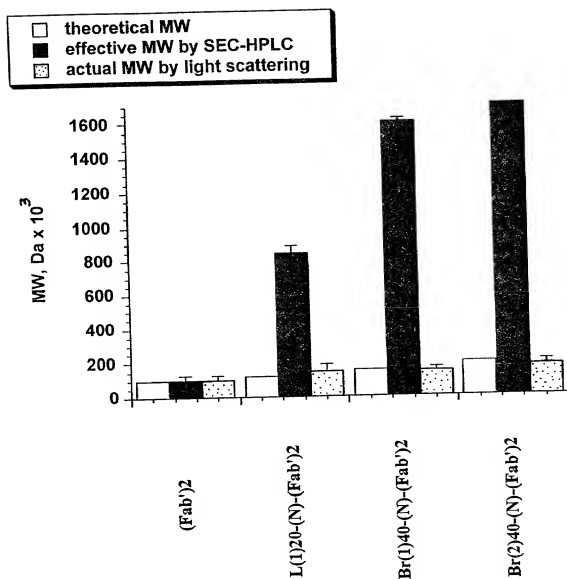
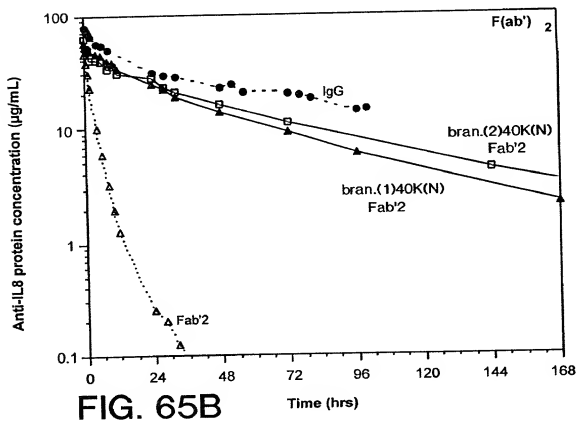
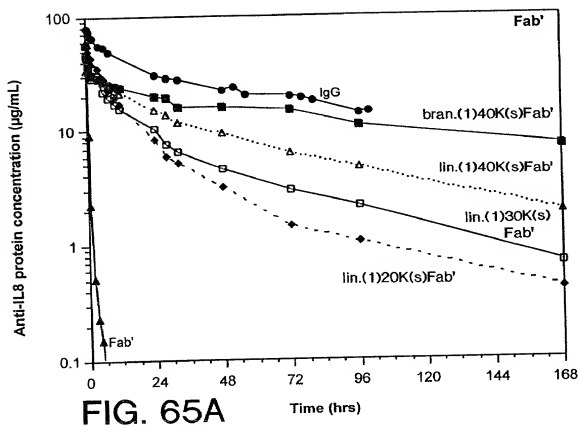


FIG. 63



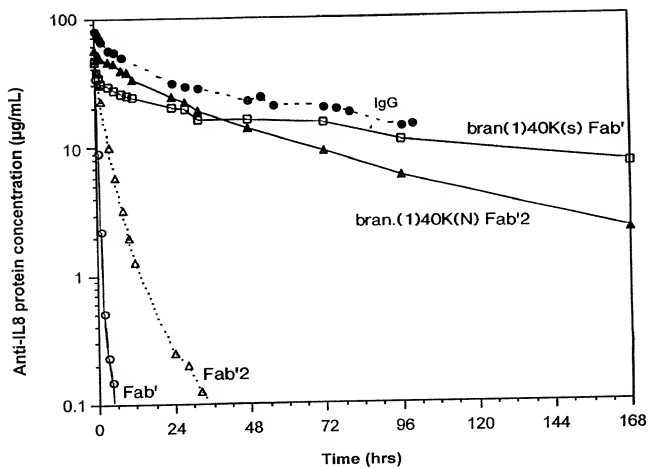


FIG. 66

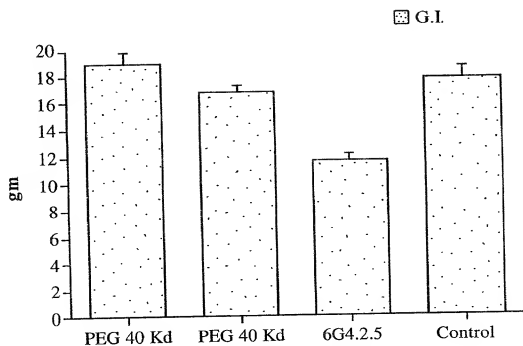


FIG. 67

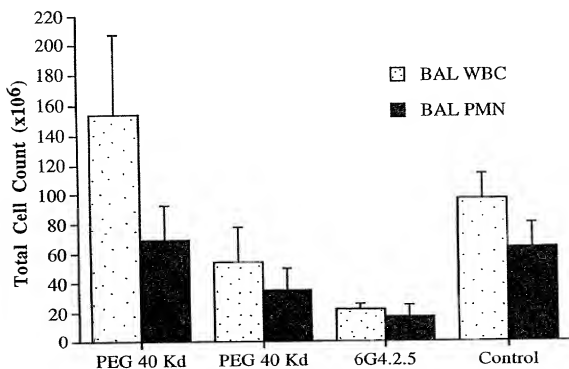


FIG. 68

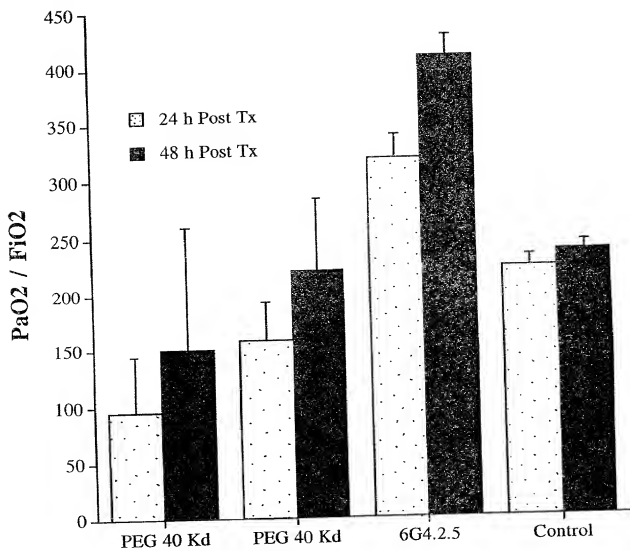


FIG. 69

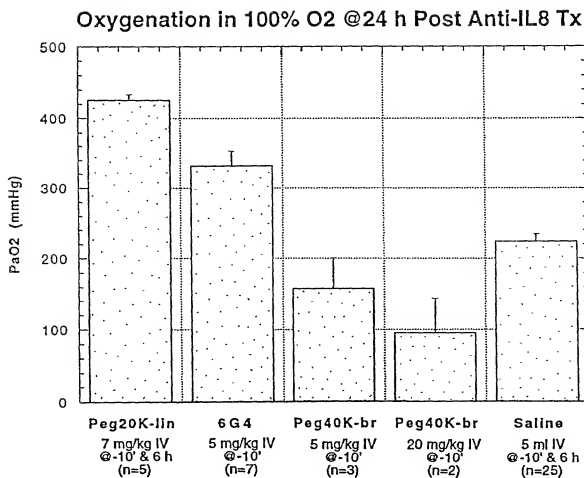


FIG. 70A

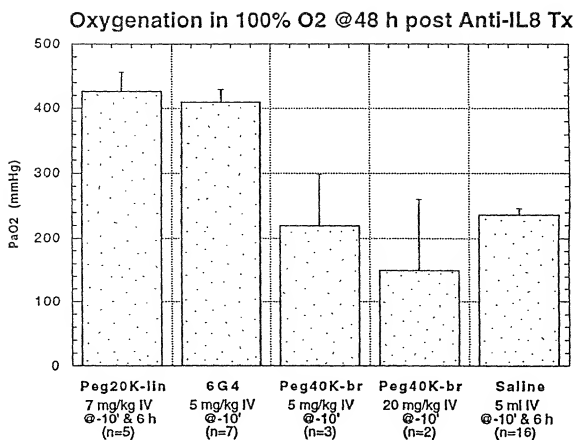


FIG. 70B

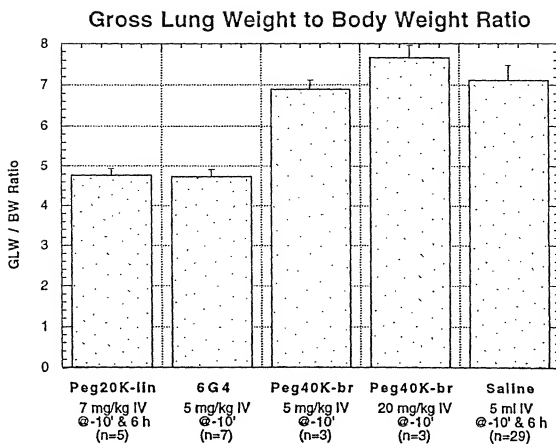


FIG. 70C

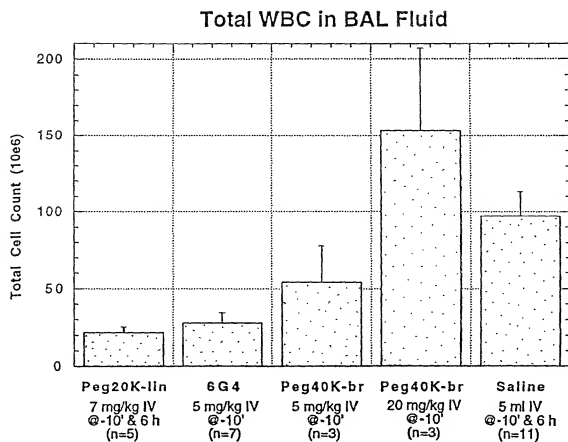


FIG. 70D

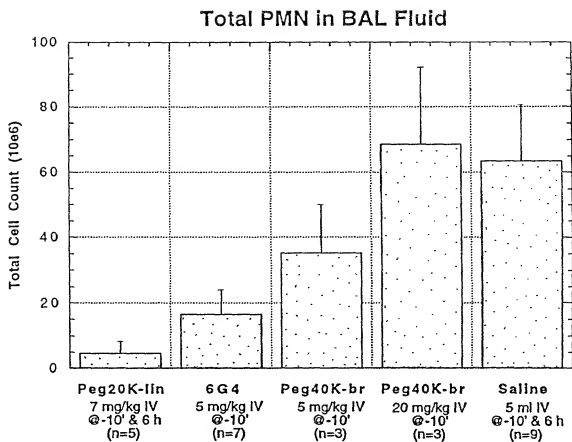
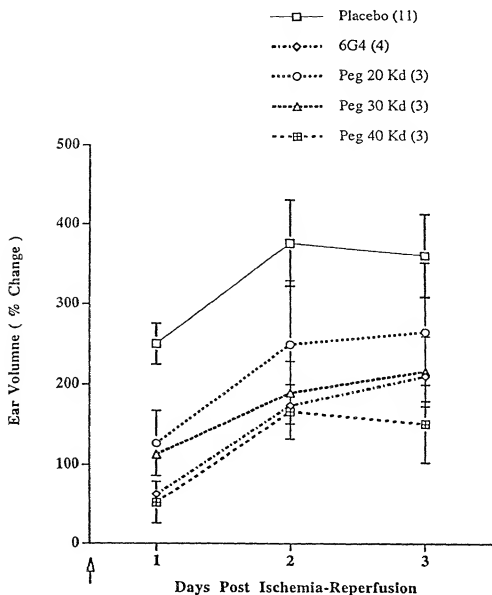


FIG. 70E

The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations :
Single Dose (5 mg/kg)
administered IV at time
of reperfusion

FIG. 71